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| (54) Title: <b>CROSSLINKING OF POLYETHYLENE FOR LOW WEAR USING RADIATION AND THERMAL TREATMENTS</b>   |  |  |   |
| (57) Abstract   |  |  |   |
| <p>The present invention discloses methods for enhancing the wear-resistance of polymers, the resulting polymers, and <i>in vivo</i> implants made from such polymers. One aspect of this invention presents a method whereby a polymer is irradiated, preferably with gamma radiation, then thermally treated, such as by remelting or annealing. The resulting polymeric composition preferably has its most oxidized surface layer removed. Another aspect of the invention presents a general method for optimizing the wear resistance and desirable physical and/or chemical properties of a polymer by crosslinking and thermally treating it. The resulting polymeric composition is wear-resistant and may be fabricated into an <i>in vivo</i> implant.</p> |  |  |   |

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CROSSLINKING OF POLYETHYLENE FOR LOW WEAR  
USING RADIATION AND THERMAL TREATMENTS

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This application is based on U.S. provisional applications: serial number 60/017,852 filed on July 9, 1996; serial number 60/025,712 filed on September 10, 1996; and U.S. provisional application, "Crosslinking of Polyethylene for Low Wear Using Radiation and Thermal Treatments", of Fu-Wen Shen et al., with attorney docket number 5910-108P3 (correct serial number not yet assigned), filed on April 29, 1997.

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Technical Field Of The Invention

20

The present invention relates to polymers. It discloses methods for enhancing the wear-resistance of polymers by crosslinking and thermally treating them. The polymers disclosed herein are useful for making implants, for example, as components of artificial joints such as acetabular cups.

25

Background Of The Invention

30

Ultrahigh molecular weight polyethylene (hereinafter referred to as "UHMWPE") is commonly used to make prosthetic joints such as artificial hip joints. In recent years, it has become increasingly apparent that tissue necrosis and interface osteolysis, in response to UHMWPE wear debris, are primary contributors to the long-term loosening failure of prosthetic joints. For example, wear of acetabular cups of UHMWPE in artificial hip joints introduces many microscopic wear particles into the surrounding tissues. The reaction

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to these particles includes inflammation and deterioration of the tissues, particularly the bone to which the prosthesis is anchored. Eventually, the prosthesis becomes painfully loose and must be replaced.

Improving the wear resistance of the UHMWPE socket and, thereby, reducing the rate of production of wear debris would extend the useful life of artificial joints and permit them to be used successfully in younger patients. Consequently, numerous modifications in physical properties of UHMWPE have been proposed to improve its wear resistance.

UHMWPE components are known to undergo a spontaneous, post-fabrication increase in crystallinity and changes in other physical properties. {See e.g., Rimnac, C.M., et al., J. Bone & Joint Surgery, 76-A(7):1052-1056 (1994)}. These changes occur even in stored (non-implanted) cups after sterilization with gamma radiation, which initiates an ongoing process of chain scission, crosslinking, and oxidation or peroxidation involving the free radicals formed by the irradiation. These degradative changes may be accelerated by oxidative attack from the joint fluid and cyclic stresses applied during use.

In an attempt to improve wear resistance, DePuy-DuPont Orthopaedics fabricated acetabular cups from conventionally extruded bar stock that previously had been subjected to heating and hydrostatic pressure that reduced fusion defects and increased the crystallinity, density, stiffness, hardness, yield strength, and increased the resistance to creep, oxidation and fatigue. Alternatively, silane cross-linked UHMWPE (XLP) has also been used to make acetabular cups for total hip replacements in goats. In this case, the number of in vivo debris particles appeared to be greater for XLP than conventional UHMWPE cup implants {Ferris, B.D., J. Exp. Path., 71:367-373 (1990)}.

Other modifications of UHMWPE have included: (a) reinforcement with carbon fibers; and (b) post-processing treat-

ments such as solid phase compression molding. Indeed, carbon fiber reinforced polyethylene and a heat-pressed polyethylene have shown relatively poor wear resistance when used as the tibial components of total knee prosthesis. {See e.g., Rimnac, C.M., et al., Trans. Orthopaedic Research Society, 17:330 (1992)}.

Recently, several companies have modified the method of radiation sterilization to improve the wear resistance of UHMWPE components. This has typically involved packaging the polyethylene cups either in an inert gas (e.g., Howmedica, Inc.), in a partial vacuum (e.g., Johnson & Johnson, Inc.) or with an oxygen scavenger (e.g., Sulzer Orthopaedics, Inc.).

#### Summary Of the Invention

The present invention comprises two aspects:

The first aspect of the invention presents a method for increasing the wear resistance of a polymer by crosslinking the polymer, followed by thermally treating the crosslinked polymer. Non-limiting examples of the thermal treatments are remelting or annealing. Preferably, the polymer is crosslinked by gamma irradiation in the solid state prior to being modified to a desired final form or shape of the final product. In the preferred embodiment, the surface layer of the crosslinked and thermally treated polymer, which is the most oxidized and least crosslinked part of the polymer, is removed, e.g., in the process of machining the final product out of the irradiated bar and thermally treated bar or block. The radiation dose is also preferably adjusted so that the optimal dose occurs within the solid polymer bar or block at the level of the bearing surface of the final product. Also presented are the polymers made from this method; methods for making products (e.g., in vivo implants) from these polymers; and the products (e.g., in vivo implants) made from these polymers.

20 The second aspect of the invention provides a systematic method for determining an optimal balance among wear resistance and other physical and/or chemical properties that are deemed important to the long-term performance of an implant *in vivo*, and applying this optimal balance to determine the appropriate crosslinking and thermal treatment  
25 conditions for processing a polymer. A flowchart is provided as a non-limiting illustration of the method for determining the optimal balance. Also provided are methods for treating polymers which apply the above appropriate crosslinking and thermal treatment conditions; the polymers produced by these  
30 methods; methods for making products (e.g., *in vivo* implants) from these polymers; and the products (e.g., *in vivo* implants) made from these polymers.

#### Brief Description Of The Drawings

35 FIG. 1 presents the degree of crystallinity vs. depth at indicated doses for UHMWPE that was irradiated in a vacuum (i.e., a low-oxygen atmosphere).

FIG. 2 presents the gel content vs. depth at indicated doses for UHMWPE that was irradiated in a vacuum (i.e., a  
40 low-oxygen atmosphere).

FIG. 3 presents the gel content vs. depth at indicated conditions for UHMWPE.

FIG. 4 presents the degree of crystallinity vs. depth at indicated conditions for UHMWPE.

45 FIG. 5 presents the gel content vs. depth at indicated conditions for UHMWPE.

FIG. 6 presents the shape of the acetabular cup fabricated from the irradiated UHMWPE.

FIG. 7 presents a schematic diagram of the hip joint  
50 simulator used in the wear tests.

FIG. 8 presents the wear by volume loss of each cup of the four materials. Upper curves: 3.3 Mrad; Lower curves: 28 Mrad.

FIG. 9 presents the curves of the average volumetric wear and standard deviations of three cups of each material at each interval.

FIG. 10 presents the oxidation profile as a function of depth at various aging times.

FIG. 11 presents the oxidation profile as a function of depth at various aging times.

FIG. 12 presents the oxidation profile as a function of depth at various aging times.

FIG. 13 presents the oxidation profile as a function of depth at various aging times.

FIG. 14 presents the oxidation profile as a function of depth for various materials. The specimens were stored in air for 5 months and then aged for 20 days at 80°C.

FIG. 15 presents gel content as a function of depth at various aging times.

FIG. 16 presents gel content as a function of depth at various aging times.

FIG. 17 presents gel content as a function of depth at various aging times.

FIG. 18 presents gel content as a function of depth at various aging times.

FIG. 19 presents the degree of crystallinity as a function of depth after 30 days' aging.

Fig. 20 shows the combined soak-corrected wear for the non-aged and aged cups.

Fig. 21 shows the individual wear for cups irradiated at different doses.

Fig. 22 shows the average wear rate versus radiation dose of non-remelted and remelted cups.

Figs. 23A and 23B present the flowchart illustrating the optimization method of the present invention.

Fig. 24 graphically shows the oxidation profiles for irradiated and remelted UHMWPE as a function of depth from the UHMWPE bar surface.

Fig. 25 graphically shows the tensile strength at yield versus radiation dose of irradiated UHMWPE with or without remelting, and non-irradiated and not remelted UHMWPE.

Fig. 26 graphically shows the tensile strength at break versus radiation dose of irradiated UHMWPE with or without remelting, and non-irradiated and not remelted UHMWPE.

Fig. 27 graphically shows the elongation at break versus radiation dose of irradiated UHMWPE with or without remelting, and non-irradiated and not remelted UHMWPE.

#### Detailed Description Of The Invention

Abbreviations used in this application are as follows:

UHMW -- ultra-high molecular weight  
UHMWPE -- ultra-high molecular weight polyethylene  
HMW -- high molecular weight  
HMWPE -- high molecular weight polyethylene

The present invention contains two aspects. The first aspect of the invention provides methods for improving the wear resistance of a polymer by crosslinking (preferably the bearing surface of the polymer) and then thermally treating the polymer, and the resulting novel polymer. Preferably, the most oxidized surface of the polymer is also removed. Also presented are the methods for using the polymeric compositions for making products and the resulting products, e.g., in vivo implants. Specific examples of this method are presented in the section: "I. First Aspect of the Invention: Polymeric Compositions with Increased Wear Resistance" and "I (A) Further Examples of the First Aspect of the Invention", below.

The method of the invention utilizes irradiation for crosslinking a polymer followed by thermal treatment to decrease the free radicals to produce a preformed polymeric composition. The term "preformed polymeric composition" means that the polymeric composition is not in a final



desired shape or form (i.e., not a final product). For  
20 example, where the final product of the preformed polymeric  
composition is an acetabular cup, irradiation and thermal  
treatment of the polymer could be performed at pre-acetabu-  
lar cup shape, such as when the preformed polymeric composi-  
tion is in the form of a solid bar or block.

25 A second aspect of the invention provides a systematic  
method (an example of which is illustrated in the flowchart,  
below) for determining the optimal parameters for the above  
mentioned crosslinking and thermal treatment. This second  
30 aspect provides a method for determining the maximum possi-  
ble improvement in wear resistance, consistent with keeping  
the other physical and/or chemical propert(ies) within the  
user's desired limits, with the least amount of trial and  
error testing. Once the optimal parameters (i.e.,  
35 crosslinking conditions such as radiation dose when radia-  
tion is used to crosslink the polymer, and thermal treatment  
parameters) are determined by this method, the polymer will  
then be processed according to the optimal parameters. Thus,  
this protocol renders the development of a preformed poly-  
40 meric composition with particular chemical/mechanical char-  
acteristics routine without resort to undue experimentation.  
Also presented are the methods for using the preformed  
polymeric composition for making products, and the products,  
e.g., in vivo implants.

45 In the present invention, the wear resistance of the  
polymer is improved by crosslinking. The crosslinking can  
be achieved by various methods known in the art, for exam-  
ple, by irradiation from a gamma radiation source or from an  
electron beam, or by photocrosslinking. The preferred method  
for crosslinking the polymer is by gamma irradiation. The  
50 polymer is preferably crosslinked in the form of an extruded  
bar or molded block.

In the preferred method, the crosslinked polymer is  
subjected to thermal treatment such as by remelting (i.e.,

20 heated above the melting temperature of the crosslinked polymer) or annealing (i.e., heated at below the melting temperature of the crosslinked polymer) to produce the preformed polymeric composition.

25 In the preferred embodiment of both the first and second aspects of the invention, the outer layer of the resulting preformed polymeric composition, which is generally the most oxidized and least crosslinked and, thus, least wear resistant, is removed. For example, the bearing surface of the preformed polymeric composition may be fashioned from inside, e.g., by machining away the surface of  
30 the irradiated and thermally treated composition before or during fashioning into the final product, e.g., into an implant. Bearing surfaces are surfaces which are in moving contact with another, e.g., in a sliding, pivoting, or rotating relationship to one another.

35

#### Choices of Polymers

The polymers are generally polyester, poly(methylmethacrylate), nylon, polycarbonates, and polyhydrocarbons such as polyethylene, and polypropylene.  
40 High molecular weight (HMW) and ultra-high molecular weight (UHMW) polymers are preferred, such as HMW polyethylene (HMWPE), UHMW polyethylene (UHMWPE), and UHMW polypropylene. HMW polymers have molecular weights ranging from about  $10^5$  grams per mole to just below  $10^6$ . UHMW polymers have molecular weights equal to or higher than  $10^6$  grams per mole,  
45 preferably from  $10^6$  to about  $10^7$ . The polymers are generally between about 400,000 grams per mole to about 10,000,000 and are preferably polyolefinic materials.

50 For implants, the preferred polymers are those that are wear resistant and have exceptional chemical resistance. UHMWPE is the most preferred polymer as it is known for these properties and is currently widely used to make acetabular cups for total hip prostheses and components of

20 other joint replacements. Examples of UHMWPE are those  
having molecular weight ranging from about  $1$  to  $8 \times 10^6$   
grams per mole, examples of which are: GUR 4150 or 4050  
(Hoechst-Celanese Corporation, League City, Texas) with a  
weight average molecular weight of  $5$  to  $6 \times 10^6$  grams per  
mole; GUR 4130 with a weight average molecular weight of  $3$   
25 to  $4 \times 10^6$ ; GUR 4120 or 4020 with a weight average molecular  
weight of  $3$  to  $4 \times 10^6$ ; RCH 1000 (Hoechst-Celanese  
Corp.) with a weight average of molecular weight of  $4 \times 10^6$   
and HiFax 1900 of  $2$  to  $4 \times 10^6$  (HiMont, Elkton, Maryland).  
Historically, companies which make implants have used  
30 polyethylenes such as HIFAX 1900, GUR 4020, GUR 4120 and GUR  
4150 for making acetabular cups.

#### Sterilization Methods

35 All polymeric products must be sterilized by a suitable  
method prior to implanting in the human body. For the formed  
crosslinked and thermally treated polymeric compositions  
(i.e., the final products) of the present invention, it is  
preferable that the products be sterilized by a non-radia-  
tion based method, such as ethylene oxide or gas plasma, in  
40 order not to induce additional crosslinking and/or oxidation  
of the previously treated preformed polymeric composition.  
Compared to radiation sterilization, a non-radiation steril-  
ization method has a minor effect on the other important  
physical characteristics of the product.

45 Nevertheless, the method can be used in conjunction  
with radiation sterilization. If the final products are to  
be sterilized by an additional dose of radiation, it is  
preferable to take into account the effect of this addi-  
tional radiation dose on the wear resistance and other  
50 properties of the polymer, in determining the optimum radia-  
tion dose used in the initial crosslinking. Furthermore, it  
is preferable that the radiation sterilization be done while  
the final product (e.g., in vivo implant) is packed in a

suitable low-oxygen atmosphere (e.g., in partial vacuum, in  
20 an inert gas such as nitrogen, or with an oxygen scavenger  
included) in order to minimize oxidation of the surface  
layer of the final product during and after sterilization by  
irradiation.

The dose ranges in this application do not take into  
25 account radiation sterilization. If radiation sterilization  
is used, then the dose ranges may have to be adjusted. Such  
adjustment can be easily performed using the teachings  
herein. For example, if after comparing the dose-response  
curves for wear with those for other important physical or  
30 chemical properties, it is determined that the optimal total  
radiation dose is 8 Mrad, and it is intended to sterilize  
the polymer with 2.5 Mrad gamma radiation (the minimum  
industrial standard sterilization dose), then the initial  
radiation dose (before sterilization) should be 5.5 Mrad,  
35 such that the total dose (initial plus sterilization doses)  
will be 8 Mrad. These calculations are approximate, since  
the total crosslinking achieved will not be exactly equiva-  
lent to a single 8 Mrad dose.

Nevertheless, the applicants have discovered that a  
40 high level of crosslinking in the surface layer of a polymer  
markedly reduces the degradative effects of surface oxida-  
tion, i.e., that would otherwise occur if a non-pre-  
crosslinked polymer were irradiated in the presence of  
oxygen (for example, see Fig. 3).

#### 45 Methods for Characterizing the Polymers

The degree of crystallinity can be determined using  
methods known in the art, e.g. by differential scanning  
calorimetry (DSC), which is generally used to assess the  
50 crystallinity and melting behavior of a polymer. Wang, X. &  
Salovey, R., J. App. Polymer Sci., 34:593-599 (1987).

Wide-angle X-ray scattering from the resulting polymer  
can also be used to further confirm the degree of

20 crystallinity of the polymer, e.g. as described in Spruiell,  
J.E., & Clark, E.S., in "Methods of Experimental-Physics",  
L. Marton & C. Marton, Eds., Vol. 16, Part B, Academic  
Press, New York (1980). Other methods for determining the  
degree of crystallinity of the resulting polymer may include  
25 Fourier Transform Infrared Spectroscopy {Painter, P.C. et  
al., "The Theory Of Vibrational Spectroscopy And Its Appli-  
cation To Polymeric Materials", John Wiley and Sons, New  
York, U.S.A. (1982)} and density measurement (ASTM D1505-  
68). Measurements of the gel content and swelling are gener-  
ally used to characterize crosslink distributions in poly-  
30 mers, the procedure is described in Ding, Z.Y., et al., J.  
Polymer Sci., Polymer Chem., 29:1035-38 (1990). FTIR can  
also be used to assess the depth profiles of oxidation as  
well as other chemical changes such as unsaturation {Nagy,  
E.V., & Li, S., "A Fourier transform infrared technique for  
35 the evaluation of polyethylene orthopaedic bearing materi-  
als", Trans. Soc. for Biomaterials, 13:109 (1990); Shinde,  
A. & Salovey, R., J. Polymer Sci., Polym. Phys. Ed.,  
23:1681-1689 (1985)}.

#### 40 Use of Crosslinked Polymers for Implants

Another aspect of the invention presents a process for  
making implants using the preformed polymeric composition of  
the present invention. The preformed polymeric composition  
may be shaped, e.g., machined, into the appropriate implants  
45 using methods known in the art. Preferably, the shaping  
process, such as machining, removes the oxidized surface of  
the composition.

#### Preformed Polymeric Compositions

50 The preformed polymeric compositions of the present  
invention can be used in any situation where a polymer,  
especially UHMWPE, is called for, but especially in situa-  
tions where high wear resistance is desired. More particu-

larly, these preformed polymeric compositions are useful for  
20 making implants.

#### Implants Made of Crosslinked Polymers

An important aspect of this invention presents implants  
that are made with the above preformed polymeric composi-  
25 tions or according to the methods presented herein. In  
particular, the implants are produced from preformed poly-  
meric composition are UHMW polymers crosslinked by gamma  
radiation followed by remelting or annealing, removing the  
oxidized surface layer and then fabricating into a final  
30 shape. The preformed polymeric composition of the present  
invention can be used to make implants for various parts of  
the body, such as components of a joint in the body. For  
example, in the hip joints, the preformed polymeric composi-  
tion can be used to make the acetabular cup, or the insert  
35 or liner of the cup, or trunnion bearings (e.g. between the  
modular head and the stem). In the knee joint, the pre-  
formed polymeric compstition can be used to make the tibial  
plateau (femoro-tibial articulation), the patellar button  
(patello-femoral articulation), and trunnion or other bear-  
40 ing components, depending on the design of the artificial  
knee joint. In the ankle joint, the preformed polymeric  
composition can be used to make the talar surface (tibio-  
talar articulation) and other bearing components. In the  
elbow joint, the preformed polymeric composition can be used  
45 to make the radio-numeral joint, ulno-humeral joint, and  
other bearing components. In the shoulder joint, the pre-  
formed polymeric composition can be used to make the  
glenoro-humeral articulation, and other bearing components.  
In the spine, the preformed polymeric composition can be  
50 used to make intervertebral disk replacement and facet joint  
replacement. The preformed polymeric composition can also  
be made into temporo-mandibular joint (jaw) and finger

20 joints. The above are by way of example, and are not meant to be limiting.

The following discusses the first and second aspects of the invention in more detail.

25 I. First Aspect of the Invention: Polymeric Compositions with Increased Wear Resistance

30 The first aspect of the invention provides preformed polymeric compositions which are wear resistant and useful for making *in vivo* implants. In this aspect, for polymers in general, and more preferably UHMW and HMW polymers, and most preferably UHMWPE and HMWPE, the irradiation dose is preferably from about 1 to about 100 Mrad, and more preferably, from about 5 to about 25 Mrad, and most preferably from about 5 to about 10 Mrad. This most preferable range is  
35 based on achieving what the inventors have determined to be a reasonable balance between improved wear resistance and minimal degradation of other important physical properties.

40 *In vivo* implants of the present invention, i.e., irradiated within the above dose ranges are expected to function *in vivo* without mechanical failure. The UHMWPE acetabular cups used by Oonishi et al. [in Radiat. Phys. Chem., 39: 495-504 (1992)] were irradiated to 100 Mrad and functioned *in vivo* without reported mechanical failure after as long as 26 years of clinical use. Furthermore, it is surprising  
45 that, as shown in the EXAMPLES, acetabular cups from the preformed polymeric composition prepared according to the present invention, but irradiated to much less than 100 Mrad, exhibited much higher wear resistance than reported by Oonishi et al.

50 On the other hand, if a user is primarily concerned with reducing wear, and other physical properties are of secondary concern, then a higher dose than the above stipulated most preferable range (e.g., 5 to 10 Mrad) may be

appropriate, or vice versa (as illustrated in the detailed  
20 examples in the following section). The optimum radiation  
dose is preferably based on the dose received at the level  
of the bearing surface in the final product. Gamma radiation  
is preferred.

The irradiated polymer is then preferably remelted at  
25 or above melting temperature of the irradiated polymer,  
e.g., in air. As used herein, the melting temperature of  
the crosslinked or irradiated polymer is identified from the  
peak of the melting endotherm as measured by DSC. Prefera-  
bly, the remelting temperature is from about the melting  
30 temperature of the irradiated polymer to about 100°C to  
about 160°C above the melting temperature of the irradiated  
polymer; more preferably from about 40°C to about 80°C above  
the melting temperature of the irradiated polymer; and most  
preferably from about 1°C to about 60°C above the melting  
35 temperature of the irradiated polymer. For example, in the  
case of UHMWPE, the remelting temperature is preferably from  
about 136°C to about 300°C, more preferably from about 136°C  
to about 250°C, and most preferably from about 136°C to  
about 200°C. Specific conditions for remelting are described  
40 in EXAMPLES 1 and 2, below.

Generally, in practice, the remelting temperature is  
inversely proportional to the remelting period. The polymer  
is preferably remelted over a period from about 1 hour to  
about 2 days, more preferably from about 1 hour to about 1  
45 day, and most preferably from about 2 hours to about 12  
hours.

Since, depending on the time and temperature applied,  
annealing can produce less of an effect than remelting on  
physical properties such as crystallinity, yield strength  
50 and ultimate strength, annealing may be used in place of  
remelting as a means for reducing the free radicals remain-  
ing in the polymer after irradiation crosslinking, in order  
to maintain these physical properties within limits required



by the user. Thermal treatment, such as remelting or annealing, removes free radicals and thereby improves long term wear resistance of the polymer. On the other hand, annealing is slower and thus takes longer than remelting, making it likely to be more expensive in industrial applications.

The annealing temperature is preferably from about room temperature to below the melting temperature of the irradiated polymer; more preferably from about 90°C to about 1°C below the melting temperature of the irradiated polymer; and most preferably from about 60°C to about 1°C below the melting temperature of the irradiated polymer. For example, UHMWPE may be annealed at a temperature from about 25°C to about 135°C, preferably from about 50°C to about 135°C, and more preferably from about 80°C to about 135°C. The annealing period is preferably from about 2 hours to about 7 days, and more preferably from about 7 hours to about 5 days, and most preferably from about 10 hours to about 2 days.

Instead of using the above range of radiation dose as a criterion, the appropriate amount of crosslinking may be determined based on the degree of swelling, gel content, or molecular weight between crosslinks after thermal treatment. This alternative is based on the applicant's findings (detailed below) that acetabular cups made from UHMWPE falling within a preferred range of these physical parameters have reduced or non-detectable wear. The ranges of these physical parameters include one or more of the following: a degree of swelling of between about 1.7 to about 5.3; molecular weight between crosslinks of between about 400 to about 8400 g/mol; and a gel content of between about 95% to about 99%. A preferred polymer or final product has one or more, and preferably all, of the above characteristics. These parameters can also be used as starting points in the second aspect of the invention (as illustrated by the flowchart, discussed below) for determining the desired radiation dose to balance the improvement in wear resistance with other

desired physical or chemical properties, such as polymer strength or stiffness.

After crosslinking and thermal treatment, preferably, the most oxidized surface of the preformed polymeric composition is removed. The depth profiles of oxidation of the preformed polymeric composition can be determined by methods known in the art, such as FTIR, described above and in EXAMPLES 3 and 6. In general, to remove the most oxidized surface, preferably a minimum of about 0.5 mm to 1.0 mm of the surface of preformed polymeric composition which is exposed to air is removed, e.g. by machining, before or while fashioning the preformed polymeric composition into the final product.

I. (A) Further Examples of the First Aspect of the Invention

As noted above, the most preferable range of dose for crosslinking radiation (i.e., from 5 to 10 Mrad) was based on achieving what the inventors have determined to be a reasonable balance between improved wear resistance and minimal degradation of other important physical properties. The following examples illustrate applications of the present invention with alternative criteria for the optimal dose. These examples use *in vivo* implants as non-limiting examples of the products, and UHMWPE or HMWPE bar or block as a non-limiting example of a starting material.

In the first example, the user desires to achieve a minimum wear rate of the *in vivo* implant made from the UHMWPE and HMWPE, and the other physical or chemical properties are important but of lesser concern. In such a case, the user may choose to irradiate the UHMWPE and HMWPE bar or block between about 15 Mrad to about 20 Mrad (as shown by Fig. 22). As discussed in the section "II(b) Application of the Flowchart", below, GUR 4150 is representative of UHMWPE and HMWPE. The irradiated UHMWPE or HMWPE bar or block is further remelted or annealed at a temperature and time

described in "I. First Aspect of the Invention: Polymeric Compositions with Increased Wear Resistance", above.

In a second example, the user may wish to produce an UHMWPE which is as wear resistant as possible while meeting the tensile strength at break (ultimate), tensile strength at yield, and elongation at break criteria of the standard specified by the American Society for Testing and Materials F-648 standard (hereinafter referred to as "ASTM F648") for UHMWPE for in vivo use. The information about this standard can be found in a current issue of the Annual Book of ASTM Standards, Medical Devices and Services, "Standard Specification for Ultra-High-Molecular-Weight Polyethylene Powder and Fabricated Form for Surgical Implants", American Society for Testing and Materials. The method of the second aspect of the present invention (as illustrated by the flowchart) may be used to adjust the crosslinking and thermal treatment parameters to meet any current ASTM F648 criteria.

For example, to meet the 1996 ASTM F648 (F648-96) criteria for Type 1 or 2 UHMWPE, the UHMWPE must have: a tensile strength at break (ultimate) of at least 35 MPa (for Type 1) and 27 MPa (for Type 2) at 23°C and 5.08 cm/min; a tensile strength at yield of at least 21 MPa (Type 1) and 19 MPa (for Type 2) at 23°C, and 5.08 cm/min; and elongation at break of at least 300% at 5.08 cm/min. The test conditions are described in ASTM D638, Type IV (Annual Book of ASTM Standards, American Society for Testing and Materials).

Alternatively, to meet the 1996 ASTM F648 criteria for Type 3 UHMWPE, the UHMWPE must have: a tensile strength at break (ultimate) of at least 27 MPa at 23°C and 5.08 cm/min; a tensile strength at yield of at least 19 MPa at 23°C, and 5.08 cm/min; and elongation at break of at least 250% at 5.08 cm/min.

The plots of mechanical properties vs irradiation dose for GUR 4150 (which is representative of Type 2 UHMWPE) (Figs. 25-27) show that, for all of the radiation

20 doses between 5 to 25 Mrad, the above ASTM F648 criteria for  
Types 2 UHMWPE are fulfilled except for the elongation at  
break, which crosses the 300 limit at about 6 Mrad. Thus, if  
the ASTM F648 criteria are to be met for Types 2 UHMWPE, the  
maximum (i.e., the most preferred) gamma radiation dose is  
25 about 6 Mrad. As illustrated in the second aspect of the  
invention (following section), the corresponding curves of  
wear and other physical properties vs. crosslinking dose  
could be used to determine the preferred dose range for  
other Types of UHMWPE or for other polymers in general.

30 II. Second Aspect of the Invention: Method for Optimizing  
Wear Resistance and Desirable Physical and/or Chemical  
Characteristics of a Polymeric Composition

35 The second aspect of the invention uses the findings in  
this patent application (including those presented in the  
"EXAMPLES" section, below) to construct a method which  
allows one skilled in the art, to systematically identify  
the conditions necessary to routinely produce a polymer with  
an optimal balance of wear resistance and physical and/or  
40 chemical properties, with minimal additional testing and  
minimal trial and error. In one embodiment of this aspect  
of the invention, the optimizing method can be schematically  
illustrated in a flowchart. Once the optimal conditions have  
been determined by this method, the polymer can then be  
45 subjected to these conditions for processing.

The present invention is based in part, on the discov-  
ery that wear rate decreases with increasing radiation dose,  
and there is a maximum dose above which there is little or  
no additional improvement in wear, but higher doses might  
50 degrade other important physical and/or chemical properties  
of the polymer, such as yield or ultimate strength, elonga-  
tion to failure, impact strength or fatigue resistance, as  
well as increasing the susceptibility to oxidation. Oxida-

tion, in turn, is known to adversely affect one or more of these physical properties, and was shown to occur in the examples below for UHMWPE crosslinked at a dose averaging about 28 Mrad if there had been no thermal treatment. Consequently, a polymer irradiated at a high radiation dose may exhibit improved wear resistance, but its other physical or chemical properties may fall outside of desirable or allowable limits, such as those specified by ASTM F648 for UHMWPE for in vivo use.

The method is also based in part on the discovery that, while other important physical properties (such as crystallinity or elongation to break) may be markedly affected by the amount of thermal treatment (e.g., remelting or annealing) applied to the polymer after irradiation crosslinking, the wear resistance is not markedly affected. This latter discovery permits reducing the amount of additional testing required by the user in order to identify the crosslinking dose which will provide the user's desired balance among wear resistance and other physical properties. This method is useful, e.g., in the case where performed polymeric composition made of UHMWPE is used for making in vivo implants, such as acetabular cups.

## II (a) Summary of the Steps of the Optimization Method

Thus, the second aspect of the present invention provides a systematic method for optimizing the balance among wear resistance and other desired physical and/or chemical characteristics of a polymer. The steps in this method are summarized in the non-limiting example of the flowchart of Figs. 23A and 23B. In the flowchart and the following discussion, for ease of discussion, irradiation is used as an example of a crosslinking method, and implant is used as an example of the product that is made from the polymer. However, as discussed elsewhere in this application, other crosslinking methods and products may be used.

20     Step 1: The process typically begins with the polymer in solid form, such as an extruded bar or block.

25     Step 2: The bar is irradiated over a range of doses up to the maximum that is likely to produce a material with the desired wear resistance and physical and/or chemical properties. This irradiation may be done, for example, in the case of gamma radiation by means of a cobalt 60 gamma radiation facility as is presently used for industrial-scale sterilization of implants.

30

Step 3: The irradiated bars are then remelted.

Applicants found that remelting of an irradiated polymer would substantially reduce the free radicals produced during irradiation, thus minimizing long-term oxidation and chain scission. By improving the polymeric composition's resistance to long-term oxidation, remelting also improves the polymeric composition's long-term resistance to wear. For further discussion of the subject, see EXAMPLES 2, 3, and 4, below

40

Although the bar may be contained in a low-oxygen atmosphere during the remelting, this may not be essential since, even if the bar is remelted in ambient air, the resultant oxidation may affect only the surface layer of the polymer (e.g. in the following EXAMPLE section, Figs. 2, 5, and 24, show oxidation extending to about 1 mm deep). In the preferred embodiment of the invention, the oxidized surface layer of the preformed polymeric composition will be removed, e.g., during subsequent machining of the products out of the treated bar.

50

Step 4A The radiation dose is correlated with the wear resistance of the products made from the irradiated remelted polymeric composition, as determined in a wear test that

adequately simulates the wear conditions of the products.  
For example, if the polymeric composition will be made into  
an implant, then the wear test should preferably adequately  
simulate the wear conditions of such implants *in vivo*. The  
correlation may be arrived at by plotting a dose-response  
curve for irradiation dose vs. wear.

Step 4B: Similarly, the radiation dose is correlated with  
each of the physical and/or chemical properties that may be  
markedly affected by the radiation dose and that might, in  
turn, substantially affect the performance of the implant *in*  
*vivo*, both for non-remelted and remelted polymer. Again,  
the correlation may be arrived at by plotting a dose-re-  
sponse curve for irradiation dose vs. each of these physical  
and/or chemical properties.

The user does not have to do dose vs. properties for  
each property that might be affected, but only those proper-  
ties that are considered important for the proper function-  
ing of the implant *in vivo*. Which of these properties are  
important for the intended application, and the limiting  
values of these properties, may vary for different polymeric  
compositions and for different types of applications (e.g.,  
hip prostheses compared to knee prostheses) and must, there-  
fore, be established by the user before applying the  
flowchart.

Step 5 is the first attempt at optimization. The user may  
first decide on the desired amount of improvement in the  
wear resistance, i.e., the maximum wear rate that is permis-  
sible for the user's application. The dose-response curve  
for wear (Step 4A) then shows the minimum radiation dose  
necessary to provide this amount of improvement in wear  
resistance.

Similarly, the dose response curves for the other  
physical or chemical properties deemed critical or important

(Step 4B) provide the values of these properties corresponding to the specific radiation dose identified in Step 4A as being necessary to provide the desired improvement in wear resistance. If each of these other physical or chemical properties are within allowable limits for the crosslinked and remelted polymer, then an optimal method has been identified (Step 6). In other words, the implant can be made by irradiating the solid polymer bar, remelting the bar and machining out the implant; the entire process being conducted such that the resulting implant has received the optimal dose at its bearing surface.

Alternatively, the user may first decide on critical values for one or more properties, such as ultimate tensile strength, fatigue strength, etc., and then check the corresponding dose response curves for the remelted polymer for the maximum allowable dose, and then check the wear vs. dose curve to determine whether this dose gives sufficient improvement in wear (i.e., the user does not necessarily have to begin by choosing the desired amount of improvement in wear).

However, if not enough improvement in wear will be obtained while keeping these other chemical and physical properties within allowable limits, or conversely, if the dose required for the desired wear improvement causes one or more of these properties to be out of allowable limits, then the user can use a lower radiation dose (i.e., accept a higher wear rate) if he wishes to remelt the materials or, alternatively, annealing may be substituted for remelting (Step 7). For a crosslinked material, annealing is less efficient than remelting in removing free radicals, but may cause less of a reduction in other important physical properties.

Whether annealing is a practical option will be apparent from the dose-response curves for the non-remelted and



20 remelted polymers. That is, if the desired value of the property in question falls between the two curves (see for example, Figs. 25 and 26), then a polymer with the desired limiting value may be produced by an annealing process with an appropriate time/temperature combination.

25 It is not necessary to generate additional wear dose-response curves for each of the many possible combinations of annealing time and temperature. It is expected that the radiation dose necessary to produce the desired reduction in wear that is determined from the wear dose-response curve for remelted polymer in Step 4A, will also apply to an  
30 annealed polymer produced in Step 7.

Step 7: Anneal samples of a bar or block which have been irradiated to that dose that was identified in Step 4A as being necessary to provide the required improvement in wear  
35 resistance, at various time/temperature combinations, to produce a polymer with the critical properties between those for non-remelted and remelted materials.

Step 8: The physical or chemical propert(ies) of interest  
40 of the irradiated and annealed samples of the polymer are correlated with annealing times and temperatures.

Step 9: Using ultimate tensile strength as an example of the physical characteristic of interest, depending on the resultant curve for annealing time and/or temperature vs. ultimate strength, the radiation dose required to achieve the  
45 desired wear resistance identified in Step 4A (above) should produce a polymer with an ultimate strength within allowable limits.

50 Similar consideration should be given to each of the other important physical and/or chemical properties by generation of individual curves of these properties versus annealing time and/or temperature. If each of these proper-

ties is within allowable limits at a particular annealing  
20 time and temperature combination, then a suitable method has  
been identified (Step 10).

If an annealing process cannot be identified that  
maintains the properties within allowable limits, then the  
user may choose to accept a lower radiation dose (Step 11),  
25 i.e., to accept less of an improvement in wear resistance.  
However, if a lower radiation dose (and, therefore, a  
greater wear rate) is acceptable, then the corresponding  
physical and chemical properties should again be checked for  
the remelted polymer (using the correlation arrived earlier  
30 in Step 4B), since these may be within limits at the lower  
radiation dose.

If the properties are within limits for the remelted  
polymer at the lower radiation dose, then remelting may be  
used instead of annealing to produce a polymer with the  
35 desired improvement in wear resistance (Step 6). If not,  
then the user should proceed with annealing as before (Steps  
7 through 10 or 11) but at this lower radiation dose.

The user may wish to progressively reduce the required  
amount of radiation crosslinking (i.e., to accept still  
40 higher wear rate) until a dose is identified for which all  
of the other properties deemed essential are within the  
user's required limits. The resultant dose represents the  
maximum improvement in wear resistance obtainable within the  
user's criteria.

45

## II(b) Example Applications of the Flowchart

As starting points for the flowchart, the ranges for  
radiation doses, remelting and annealing temperatures and  
times described in section "I. First Aspect of the  
50 Invention: Polymeric Compositions with Increased Wear  
Resistance" and "I (A) Further Examples of the First Aspect  
of the Invention", above, can be used, with regard to poly-

mers in general, UHMW and HMW polymers in particular, and  
20 HMWPE and UHMWPE especially.

For ease of discussion, the following examples illustrate the application of the flowchart using UHMWPE (which also behaves similar to HMWPE) as an example of a polymer and an acetabular cup as an example of an implant. GUR 4150  
25 is representative of such a class of UHMWPE. Similarly, the description uses gamma radiation as an example for crosslinking the polymer. These examples are meant to illustrate and not meant to limit the invention.

The method described by the flowchart is applicable to  
30 other polymers, implants or other products made from such polymers, and crosslinking methods (examples of which are described elsewhere in this application), and methods for making an implant or product out of the preformed polymeric composition.

35 From the data provided by the EXAMPLES (following sections) a number of generalities were discovered that allowed simplification of the use of the flowchart, i.e., to minimize the amount of additional testing that would be required of a user wishing to apply the method to other  
40 polymers, or to the GUR4150 of the EXAMPLES but with various optimization criteria.

To establish the critical curve for the reduced in vivo wear (Step 4A), the UHMWPE bar or block is preferably irradiated in Step 2 and remelted in Step 3, in a manner and to  
45 a dose and temperature and time as described for UHMWPE in the section, "I. First Aspect of the Invention: Polymeric Compositions with Increased Wear Resistance" and "I (A) Further Examples of the First Aspect of the Invention", above.

50 In step 4A, acetabular cups are machined out of the irradiated bar and wear tested under conditions suitably representative of the intended in vivo application (e.g., by the method described in the EXAMPLES section below) to

20 establish a wear vs. radiation dose response curve for the  
specific polymer. EXAMPLE 5 and Fig 22 show a wear dose-  
response curve for gamma irradiated GUR 4150 UHMWPE.

Applicants discovered that it is not necessary to  
generate additional wear dose-response curves for each of  
the many possible combinations of annealing time and temper-  
25 ature. This follows from the results of EXAMPLE 2. Since  
annealing is done at a lower temperature than remelting and,  
therefore, has a less marked effect on physical properties  
in general, it can be expected that annealing will have even  
less of an effect on the wear resistance than remelting.

30 Another important aspect of the invention is the dis-  
covery that wear resistance of GUR 4150 was not markedly  
affected by remelting and, therefore, it is also not likely  
to be markedly affected by annealing time and temperature.  
Therefore, it is expected that the radiation dose necessary  
35 to produce the desired reduction in wear that is determined  
from the wear dose-response curve for remelted polymer in  
Step 4A, will also apply to an annealed polymer produced in  
Step 7. Therefore, while the user needs to do his own tests  
to establish tensile strength vs dose etc., he can rely on  
40 the wear vs dose curve developed for the remelted material,  
rather than running an additional set of wear curves for  
each annealing condition. This represents a considerable  
saving in experimental costs, since the tensile strength  
tests typically may be completed in a few days (using common  
45 tensile test apparatus), but the tests of wear vs dose  
require months to complete (and require highly specialized  
equipment and techniques available on only a handful of  
laboratories in the world).

Furthermore, if the user is working with GUR 4150, he  
50 can use the dose vs wear curve of Fig. 22 (as well as the  
plots of other mechanical properties, Figs. 25-27) without  
needing to run any wear or tensile tests. Finally, if he is  
working with another grade of UHMW polyethylene, he can

probably use Fig. 22, since other tests have shown that the wear resistances of these materials are very similar to GUR 4150 for a given sterilization treatment. At the least, Fig. 22 establishes the range on which the user may focus his wear vs. dose experiments for other grades of UHMW polyethylene, to minimize the testing necessary to identify the optimum dose.

For other polymers, comparable wear tests at each end of the range of interest for radiation dose could be applied to verify whether remelting or annealing also does not markedly affect their wear resistance. Nevertheless, GUR 4150 is representative of UHMWPEs, especially those useful for implants, in its physical and chemical properties, and applicants have observed that other UHMWPEs, of different molecular weights and with or without calcium stearate, such as GUR 1020 (calcium stearate free, lower molecular weight grade) behaved similarly to GUR 4150 in their wear resistance after irradiation sterilization in air. McKellop, H. et al., Trans. Society for Biomaterials, Vol. 20, pg. 43 (1997).

Further, it has been observed that, although the starting physical properties of HMWPE are different from those of UHMWPE, these differences will be substantially reduced after sufficient crosslinking. For example, they are almost equal after electron beam irradiation treatment to 300 kGy (30 Mrad), for properties like gel content, swelling and strength. Streicher, R. M., Beta-Gamma 1/89: 34-43, at p. 42, right col., fourth full paragraph. Even the wear properties were the same, after the differences in the molecular arrangement between HMWPE and UHMWPE were offset by the irradiation procedure. Thus, it is predicted that the findings based on GUR 4150 and the above discussion would be applicable to polymers in general, and to UHMW and HMW polymers, in particular, and especially HMWPE and UHMPE. Thus, the radiation, remelting and annealing ranges found

for GUR 4150 can be applied to polymers in general, and more preferably to HMW and UHMW polymers, and most preferably to HMWPE and UHMWPE; and these ranges can be used at the very least, as starting points in the flowchart for determining the specific ranges for other polymers, and the data in the "EXAMPLES" section below will facilitate the user in arriving at the proper conditions for GUR 4150, ASTM F648 Type 2 UHMWPE, and UHMWPE and HMWPE in general.

The following examples illustrate the use of these generalities in conjunction with the flowchart. In the first example, if the user is working with GUR 4150, or an UHMWPE that satisfies ASTM F648 Type 2 criteria in general, then, based on Figs. 25-27, only the elongation will fall below the ASTM limit (i.e., 300%) over the dose range of interest, i.e., 0 to 25 Mrad, and this occurs at about 6 Mrad. Thus, the maximum allowable dose is 6 Mrad and, from the wear vs dose plot (Fig. 22), it can be seen that a 6 Mrad dose will provide a wear rate of about 7 to 8 mm<sup>3</sup> per million cycles. This is about a 78% or more reduction over the 33.1 mm<sup>3</sup> per million cycles shown for non-remelted polyethylene gamma irradiated to 3.1 Mrad in air. If this reduction in wear rate is sufficient for the user's purpose, then his goal is achieved. Note however, that the elongation vs dose plot (Fig. 27) shows virtually the same behavior whether the polyethylene is remelted or not, so if the above 78% reduction is not sufficient for the user's purpose, then the user would have no choice but to increase the radiation dose, as annealing is also not likely to affect the elongation to break, for the reasons discussed above.

In a second example, a user requires a lower limit on tensile strength at break at 40 MPa, and wishes to produce a material with wear no more than 1 mm<sup>3</sup> per million cycles. The wear vs dose curve (Fig. 22) shows that a dose of about 15 Mrad is required to produce a polyethylene with the desired amount of wear resistance. However, the tensile

20 strength at fracture vs dose curve shows that the tensile  
strength at 15 Mrad for a remelted material is about 36 Mpa.  
Since this is below the user's acceptable limit of 40 Mpa,  
he can either use a smaller radiation dose and, therefore,  
accept a smaller improvement in wear rate (i.e., if he  
wishes to remelt his material) or he can try annealing  
25 instead of remelting since, depending on the  
time/temperature combination used, annealing can be expected  
to produce a polymer with a value of tensile strength be-  
tween the limits indicated by the curves for non-remelted  
and remelted polymer (Figs. 25 and 26). As shown on these  
30 figures, the tensile strength at 15 Mrad for a non-remelted  
material is about 46 Mpa, well above the user's limit of 40.  
So, with minimal trial and error, the user can identify an  
annealing time and temperature that, when applied to a  
polyethylene that has been exposed to 15 Mrad radiation, has  
35 a tensile strength of the required 40 Mpa. Again, based on  
the wear test results, the user knows that he does not have  
to re-do the wear vs dose curve for all of the various  
annealing treatments he tries, in order to identify the dose  
necessary to produce the desired improvement in wear resis-  
40 tance.

Having described the invention, the following examples  
are presented to illustrate and support the invention, and  
are not to be construed as limiting the scope of the inven-  
tion.

45

#### EXAMPLES

50 The nominal dose of radiation applied to implants at a  
commercial radiation facility typically varies within a  
range. Therefore, in the following examples, the average  
gamma radiation doses are given, such as average gamma  
radiation doses of 3.3, 26.5, and 28 Mrad. The average of  
3.3 Mrad was arrived at by averaging the minimum and maximum

20 doses, e.g., a minimum of 3.28 and a maximum of 3.45 Mrad. Similarly, for example, the average of 26.5 was based on averaging a minimum of 25.14 and a maximum of 27.70 Mrad; and the average of 28 was based on averaging a minimum of 26.01 and a maximum of 30.30 Mrad.

25 EXAMPLE 1: EFFECT OF RADIATION ATMOSPHERE AND DOSE ON THE PHYSICAL PROPERTIES OF UHMWPE

Experimental Details

30 Commercial-grade UHMWPE extruded bars (GUR 4150, Poly Hi Solidur), with a weight average molecular weight of  $5-6 \times 10^6$ , were used as received. The 8mm thick specimens were cut from the bars and irradiated with gamma-rays at room temperature either in ambient air or in a vacuum chamber at SteriGenics International (Tustin, CA) to average doses  
35 ranging from 3.3 to 250 Mrad. Radiation was delivered at a dose rate of 0.2 Mrad/hr. For 250 Mrad, the dose rate was 4 Mrad/hr. Cobalt-60 was used as a source of gamma radiation. A subset of the 8mm thick specimens that had been irradiated in vacuum was remelted in a vacuum oven by heating from room  
40 temperature to 145°C slowly (at about 0.3°C/min.) and maintaining at 145°C for one hour. After remelting, the specimens were slowly cooled to room temperature.

The physical properties of the disk specimens before and after irradiation and remelting were characterized by  
45 DSC, gel content analysis and FTIR.

Gel Content Analysis

50 The gel content of each material was analyzed as a function of depth from the surface. 100  $\mu$ m thick sections (about 50 mg) were microtomed across the specimen. Extraction of the sol-fraction was performed by boiling in p-xylene for 24 hours, with 0.5 wt% of antioxidant (2,6-di-*t*-butyl-4-methyl phenol) added to prevent oxidation. For



highly oxidized sections from the surface layer, which  
20 tended to break up during boiling, the specimens were  
wrapped in PTFE membrane filter (0.5  $\mu\text{m}$  pore size) to avoid  
loss of gel. After extraction, the specimens were de-swol-  
len in acetone and dried at 60°C in a vacuum oven to con-  
stant weight. The gel fraction was determined from the  
25 ratio of the weight of the dried-extracted material to that  
of the dry non-extracted material.

#### Differential Scanning Calorimetry (DSC)

For DSC measurements, samples were cored and microtomed  
30 into 200  $\mu\text{m}$  thick sections across the depth. Specimens (~4  
mg) were heated from 50°C at 10°C/min in a differential  
scanning calorimeter (Perkin-Elmer DSC-4) to 170°C. The  
melting temperature was identified from the peak of the  
melting endotherm. Indium was used for calibration of the  
35 temperature and heat of fusion. The heat of fusion was  
determined by comparing the area under the melting endotherm  
to the area of fusion of an indium sample having a known  
heat of fusion of 28.4 J/g, and divided by 292 J/g, the heat  
of fusion of an ideal polyethylene crystal, to get the  
40 degree of crystallinity.

#### Results and Discussion

As shown in Fig. 1, irradiation increased the  
crystallinity of the 8mm thick specimens of UHMWPE from  
45 about 55% to 60-66%, with considerable overlapping for the  
different doses. Similar changes were observed with the  
samples that were irradiated in air. The gel content (i.e.,  
the extent of crosslinking) (Fig. 2) also increased with  
increasing radiation dosage. Importantly, crosslinking  
50 increased markedly moving from the surface into the middle  
of each specimen, reaching about 92% for the 3.3 Mrad dose.  
Apparently, the oxygen present in the vacuum chamber was  
sufficient to cause the increased oxidation and decreased

crosslinking of the surface layer. Thus, our method, i.e.,  
20 of irradiating a bar and machining away the surface is more  
effective and efficient than use of a vacuum or other low  
oxygen atmosphere in producing a final product with minimal  
oxidation of the bearing surface. For reference (Fig. 3),  
chemically crosslinked polyethylene (PE) (1% peroxide, irra-  
25 diated in air) (Shen, F.W. et al. J. of Polv. Sci. Part B:  
Poly Phys 34:1063-1077 (1996)), which exhibits very low  
wear, has a gel content of about 90% at about 100 microns  
from the surface, rising to a maximum of nearly 100% in the  
center.

30 In a second phase of this example, the 8mm thick disks  
that had been irradiated in vacuum were remelted by heating  
to 145°C for one hour, and slowly cooled. This reduced the  
peak melting temperature, the degree of crystallinity and  
the crystal size. For example (Fig. 4), the crystallinity  
35 of the 3.3 Mrad specimens was reduced from the range of 60-  
65% to the range of 50-53% by remelting.

In addition, during remelting, residual free radicals  
that were formed by the irradiation apparently recombined  
and increased the total crosslinking (as evident from the  
40 increased gel content, Fig. 5). Extinguishing free radicals  
in this manner, in turn, further reduces the oxidation that  
would otherwise occur when the cups are stored on the shelf  
or exposed to body fluids after implantation.

The lower gel content (crosslinking) near the surface  
45 (Fig. 3) was due to oxidation of the surface layer at the  
time of irradiation. Thus, it can be expected that the  
polymer of the surface layer would have less wear resistance  
than that in the center of the specimen. In the method  
presented in this application, this gradient would not be  
50 present, since the surface layer would be removed during  
machining of the final implant from the irradiated bar or  
block.

The crystallinity and gel content of the irradiated 8mm thick disks, with and without remelting, are compared in Figs. 4 and 5, respectively.

EXAMPLE 2: WEAR TESTING OF RADIATION CROSSLINKED CUPS WITH AND WITHOUT REMELTING

Experimental Details

Six extruded bars of UHMWPE (GUR 4150), each 3 inches in diameter, were exposed to 3.3 or 28 Mrad of gamma radiation at a dose rate of 0.2 Mrad per hour in ambient air (SteriGenics, Inc., Tustin, CA). Two bars for each radiation dose were then remelted by heating in an oven in ambient atmosphere from room temperature to 150°C at about 0.3°C per minute and holding at 150°C for five hours, and then slow-cooling to room temperature. The crystallinity and gel content of these four materials were measured across the cross section of extra samples of each bar using differential scanning calorimetry (DSC) and gel content analysis. The results are summarized in Tables 1 and 2.

Four sets of acetabular cups were machined from bars of each of the four materials at a commercial machining shop (Bradford and Meneghini Manufacturing Co., Santa Fe Springs, CA). Each cup had a 2 inch outer diameter (O.D.) and 1.26 inch inner diameter (I.D.), and 1 inch outer radius and 0.633 inch inner radius (Fig. 6). Wear tests were run on two sets of three cups for each radiation dose that had been remelted, and two sets of three cups for each dose that had not been remelted. The bars were intentionally used with larger diameters than the final cups so that the process of machining away the outer 0.5 inches of each bar removed the most oxidized, most crystalline, least crosslinked surface layer which is about 0.5 to 1.0 mm thick. In this manner, the bearing surface of each cup consisted of material from near the center of the bar, i.e., the most crosslinked,

20 least crystalline, least oxidized region, which is predicted to be the most wear resistant.

Since acetabular cups used in patients must first be sterilized by some acceptable means, the test cups in this study were sterilized prior to wear testing using ethylene oxide at the appropriate dose for clinical implants. Ethylene oxide was chosen instead of additional gamma irradiation (e.g., 2.5-4.0 Mrad) in order to confine the results to the effects of the original 3.3 or 28 Mrad doses used to crosslink the materials.

30 Prior to wear testing, the cups were pre-soaked in distilled water for three weeks to minimize additional fluid absorption during the wear test, thereby making the weight loss method for wear measurement more accurate. For the wear test, the cups were enclosed in polyurethane molds and pressed into stainless steel holders (Fig. 7). Each holder was fitted with an acrylic chamber wall to contain the lubricant. The chambers were mounted on the hip simulator wear machine, with each cup bearing against a ball of cobalt-chromium alloy (conventional hip replacement femoral balls were used, with implant-quality surface finish). The ball-cup pairs were subjected to a physiological cyclic load with a peak load of about 2000 Newtons (Paul, JP., "Forces transmitted by joints in the human body". In Lubrication and Wear in Living and Artificial Human Joints. Proc Instn Mech Engrs 1967;181 Part 3J:8-15) and the cups were oscillated against the balls through a bi-axial 46° arc at 68 cycles per minute. Each test station on the simulator (Fig. 7) contains a self-centering unit 5, the acetabular cup 6, a dual axis offset drive block 7, a test chamber 8, serum lubricant 9 and a femoral ball 10. The arrow indicates the direction of the computer controlled simulated physiological load applied to the simulated hip joint.

50 During the test, the bearing surfaces were kept immersed in bovine blood serum to simulate lubrication in the

human body. Sodium azide at 0.2% was added to the serum to  
20 retard bacterial degradation, and 20 mM ethylene-  
diaminetetraacetic acid (EDTA) was added to prevent precipi-  
tation of calcium phosphate onto the surface of the balls  
(McKellop, H. and Lu, B., "Friction and Wear of  
Polyethylene-metal and Polyethylene-ceramic Hip Prostheses  
25 on a Joint Simulator, Transactions of the Fourth World  
Biomaterials Congress, Berlin, Apr. 1992, p. 118). A poly-  
ethylene skirt covered each test chamber to minimize air-  
borne contaminants.

At intervals of 250,000 cycles, the cups were removed  
30 from the machine, rinsed, inspected under light microscopy  
and replaced in fresh lubricant. At intervals of 500,000  
cycles, the cups were removed, cleaned, dried and weighed to  
indicate the amount of wear. After inspection under light  
microscopy, the cups were replaced on the wear machine with  
35 fresh lubricant and testing was continued to a total of  
three million cycles. One million cycles is approximately  
the equivalent of one year's walking activity of a typical  
patient.

The weight loss was corrected for the effects of fluid  
40 absorption (which masks wear) by increasing the apparent  
weight loss of the wear test cups by the mean weight gain of  
three control cups of each material that were also immersed  
in serum and cyclically loaded on a separate frame, but  
without oscillation. The corrected rate of weight loss was  
45 converted to volume loss by dividing by the approximate  
density of UHMWPE (0.94 gm/cc). The mean weight loss (after  
soak correction) and the standard deviation was calculated  
for each of the four types of materials at each weighing  
interval. The wear rate of each cup was calculated by  
50 applying linear regression to the wear data for the entire  
three million cycles. The mean wear rates and standard  
deviations also were calculated for each type of material.

### Results

20 Fig. 8 shows the soak-corrected wear (volume loss) of  
three cups of each material as a function of wear cycles.  
Fig. 9 shows the average wear (volume loss) of three cups of  
each material as a function of wear cycles. The individual  
wear rates and the mean values for each type of material are  
25 listed in Table 3. The most wear occurred with the cups  
subjected to 3.3 Mrad without remelting. These averaged  
21.1 mm<sup>3</sup> per million cycles.

The wear of the cups subjected to 3.3 Mrad with remelt-  
ing averaged 18.6 mm<sup>3</sup> per million cycles, or 12% lower wear  
30 than for the non-remelted 3.3 Mrad cups. The cups subjected  
to 28 Mrad had much lower wear rates than the 3.3 Mrad cups,  
and the rates were similar, whether or not the material had  
been remelted. That is, the average wear rate of the non-  
remelted 28 Mrad cups was about 1.2% that of the non-re-  
35 melted 3.3 Mrad controls, and the average wear rate of the  
remelted 28 Mrad cups was about 1.7% of the same controls.

### Discussion

The results of the wear test clearly demonstrated the  
40 improved wear resistance of the UHMWPE acetabular cups that  
resulted from exposure to 28 Mrad gamma radiation. Appar-  
ently, the crosslinking generated by the higher radiation  
dose reduced the wear rates to less than a few percent of  
the control value (3.3 Mrad). The minimum amount of wear  
45 debris necessary to induce clinically significant osteolysis  
and other problems in a specific patient has not been estab-  
lished, and it may vary among patients. Nevertheless, a  
material which reduces the wear rate to the very low levels  
exhibited by the 28 Mrad cups in this study would be very  
50 likely to provide a large margin of safety over currently  
used materials.

The wear curves for both of the 28 Mrad specimens  
(Figs. 8 & 9) were slightly negative on the first weighing

at 0.5 million cycles. This was most likely due to a slight under-correction for fluid absorption (that is, the wear test cups absorbed slightly more water than the soak controls, and the error between the two was greater than the weight loss due to wear, producing a negative wear value). If this assumption is correct, then the overall wear rates for the two 28 Mrad sets were somewhat smaller, and possibly closer together, than the values indicated in Table 3.

### EXAMPLE 3: ARTIFICIAL AGING OF RADIATION-CROSSLINKED UHMWPE

#### MATERIALS

Six UHMWPE (GUR 4150) extruded bars (3" diameter) were gamma irradiated in air, three bars each at 3.3 or 28 Mrad, at a dose rate of 0.2 Mrad/hour. For each radiation dose, two bars were then remelted by heating in an oven at ambient atmosphere from room temperature to 150°C at about 0.3°C/min, holding at 150°C for 5 hours and slowly cooling to room temperature, and the third bar was not remelted. A 13 mm (0.5 inch) layer of the outer diameter of the treated (remelted) and untreated (non-remelted) bars was machined away to remove the most oxidized, least crosslinked surface layer. The bars were used to produce specimens for the artificial aging tests described here and for the wear tests described in EXAMPLE 2.

To examine the effect of artificial aging on these four materials (3.3 and 28 Mrad, remelted and not remelted), 8 mm thick disks were cut from these 2 inch diameter cores and were heated in an oven slowly ( - 0.2 °C/min) to 80 °C at ambient atmosphere and held at 80°C for 10, 20 or 30 days. In addition, one acetabular cup for each of the four conditions (3.3 and 28 Mrad, remelted and not remelted) that had been fabricated at the same time as the wear test cups of

EXAMPLE 2 and stored in air for about 5 months was cut into  
20 four pieces and aged at 80°C for the same periods.

The gel content analysis and DSC method are as described in EXAMPLE 1, above.

#### Fourier Transform Infrared Spectroscopy (FTIR)

25 FTIR measurements were performed on the above specimens. Segments about 5 mm wide were cut from each polyethylene specimen and the segments were microtomed into 200  $\mu\text{m}$  thick slices. The oxidation profiles, as indicated by the carbonyl concentration, were measured using a Mattson Polar-  
30 aris FTIR (model IR 10410) with a Spectra-Tech IR plan microscope. Spectra were collected in 100  $\mu\text{m}$  steps from the surface to the middle of the specimen, using 64 scans summation at a resolution 16  $\text{cm}^{-1}$  with a MCT (Mercury Cadmium Telluride) detector. The carbonyl group concentration was  
35 indicated by the ratio of the peak height of the ketone absorption band at 1717  $\text{cm}^{-1}$  to the height of the reference band at 2022  $\text{cm}^{-1}$  ( -  $\text{CH}_2$  - vibration).

#### RESULTS

40 The oxidation profiles as a function of depth are shown in Figs. 10-13. As shown in Fig. 10 for the 3.3 Mrad, non-remelted material, oxidation increased with increasing aging time. In contrast, the 3.3 Mrad, remelted material (Fig.  
45 11) showed almost no oxidation for 10 and 20 days aging, but some oxidation for 30 days aging. However, the oxidation peak at the surface with remelting was about 50% of that at the surface without remelting (Fig. 10). For the 28 Mrad, non-remelted UHMWPE (Fig. 12), the oxidation showed a  
50 greater increase with increasing aging time than the 3.3 Mrad, un-remelted material. Again, oxidation was much lower with remelting, i.e., the 28 Mrad, remelted UHMWPE (Fig. 13) essentially exhibited no oxidation after 20 days aging (Fig.



13), and the oxidation peak at the surface after 30 days was only about 1/3 that without remelting (Fig. 12).

Similarly, with the acetabular cups stored in air for 5 months and then aged for 20 days at 80°C, the remelted materials (3.3 or 28 Mrad) showed no oxidation (Fig. 14), while the non-remelted cups (3.3 or 28 Mrad) showed substantial oxidation (Fig. 14), especially for 28 Mrad UHMWPE, and with a subsurface oxidation peak in both non-remelted materials.

Since crosslinking of UHMWPE reduces its solubility, the percent of undissolved material (gel content) is an indirect indication of the amount of crosslinking. The gel content as a function of depth for various conditions are shown in Figs. 15 to 18. As shown in Fig. 15 for 3.3 Mrad, non-remelted material, the gel content (i.e., crosslinking) decreased with increasing aging time. There was a strong gradient of gel content in the highly oxidized surface regions after 30 days aging, i.e., increasing from a minimum on the surface to a maximum about 2 mm below the surface. Near the surface, the gel content was highest (91%) in the un-aged specimen, and decreased with increasing aging time to less than about 5% in the same region for the 30 day aged specimen. In contrast, the remelted materials (Fig. 16) showed much less reduction in gel content in the surface regions than the non-remelted materials. That is, comparison of Fig. 17 (28 Mrad, non-remelted) and Fig. 18 (28 Mrad, remelted) showed that the remelted UHMWPE had much higher retention of gel content (i.e., crosslinking).

The results of the DSC measurements indicated the degree of crystallinity as a function of depth for various materials aged for 30 days at 80°C, as shown in Fig. 19. Near the surface, the degree of crystallinity was 83% for the 28 Mrad, non-remelted material after aging, compared to 65% before aging. The high level of crystallinity and increased brittleness of the surface zone of the aged mate-

rial often resulted in fragmentation of a layer about 1 mm  
20 thick during microtoming. In contrast, the 28 Mrad remelted  
material showed less increase in crystallinity in the sur-  
face regions due to aging, and no brittle zone was observed.  
Similarly, due to aging, the 3.3 Mrad non-remelted material  
exhibited an increase in crystallinity from 60% to about  
25 78%, and the surface layer was again brittle, although not  
as brittle as with the 28 Mrad, non-remelted material.

#### DISCUSSION

Irradiation of UHMWPE produces crosslinking, chain  
30 scission and the formation of free radicals. If oxygen is  
present, it may react with the free radicals to form oxi-  
dized species, leading to additional chain scission (reduc-  
tion in molecular weight) and an increase in crystallinity.  
Since polymer crystallites melt and become amorphous above  
35 the melting temperature, molecular chain movements and  
rotations are increased, favoring the recombination of free  
radicals. The results of the present experiments showed  
that remelting at 150°C apparently caused the residual free  
radicals to decay and/or to recombine to form crosslinks,  
40 leading to an increased gel content. Therefore, remelting  
is an effective way to extinguish free radicals, making the  
material less susceptible to long-term oxidation and poten-  
tially improving the long-term wear resistance, as evident  
from the results of the artificial aging experiments, where  
45 there was much less oxidation of the remelted materials.

For a crosslinked polymer, oxidative degradation  
cleaves the molecules and leads to a reduction in gel con-  
tent. This was evident in the present experiments from the  
reduced gel content after aging, particularly with the non-  
50 remelted materials (Figs. 15 to 18). That is, the distribu-  
tion of oxidation, as indicated by the profiles measured by  
FTIR, was inverse to the gel content within the material;  
the higher the oxidation, the lower the gel content

(crosslinking). Since remelting extinguishes free radicals and increases gel content, thereby reducing the susceptibility to oxidation, the remelted materials (3.3 and 28 Mrad) had a much greater gel content after artificial aging than the non-remelted materials.

An appropriate amount of crosslinking of UHMWPE can improve its wear resistance. The high level of crosslinking in the UHMWPE caused by the 28 Mrad gamma irradiation, as evident from the high gel content (EXAMPLE 2), apparently contributed to the much greater wear resistance exhibited by the acetabular cups tested in EXAMPLE 2. In addition, as shown in EXAMPLE 3, remelting of the irradiated UHMWPE markedly reduced the residual free radicals, rendering the material much more resistant to subsequent oxidation and, therefore, resistant to a reduction in crosslinking, which can be of substantial benefit for implants in long-term clinical use.

#### EXAMPLE 4: WEAR TESTING OF IRRADIATED CUPS WITH AND WITHOUT ARTIFICIAL AGING

##### Materials and Methods

The wear testing of irradiated cups with and without remelting was described in EXAMPLE 2. Effects of artificial aging on the physical properties of irradiated UHMWPE, with and without remelting, were described in EXAMPLE 3. To examine the resistance of crosslinked cups to thermal-induced oxidation, and the effect of such oxidation on the wear of irradiated cups with and without remelting, two acetabular cups for each of the four conditions (3.3 and 28 Mrad, remelted and not remelted) that had been wear tested for 3 million cycles as described in EXAMPLE 2, were heated in an oven slowly (~ 0.2 °C/min) to 80 °C at ambient atmosphere and held at 80 °C for 20 days, with one acetabular cup for each of the four conditions being stored in ambient

air. The oxidation profile after 20-day aging for each  
condition was shown in Fig. 14, EXAMPLE 3.

Prior to wear testing, the cups were pre-soaked in  
distilled water for four weeks to minimize additional fluid  
absorption during the wear test, thereby making the weight  
loss method for wear measurement more accurate. The details  
for the wear test were described in EXAMPLE 2.

### Results

Fig. 20 shows the combined soak-corrected wear (volume  
loss) for the cups before aging (3.3 and 28 Mrad, remelted  
and not remelted) during the first 3 million cycles (same  
data as EXAMPLE 2) and for the same cups, after two cups of  
each material had been artificially aged, from 3 to 7 mil-  
lion cycles. The individual wear rates and the mean values  
for each type of material, calculated by linear regression,  
are listed in Table 4.

All cups subjected to 3.3 Mrad with remelting showed  
comparable wear rates, whether or not the material had been  
remelted or remelted and aged. Wear was negligible for all  
of the cups subjected to 28 Mrad, whether or not these were  
remelted, and whether or not they were aged.

### Discussion

The results of the wear test clearly demonstrated the  
improved wear resistance of the UHMWPE acetabular cups that  
resulted from exposure to 28 Mrad gamma radiation. Appar-  
ently, the minor oxidation at the surface (Fig. 14) of the  
highly crosslinked acetabular cups (28 Mrad, without remelt-  
ing) induced by the artificial aging, had very limited  
effect on the wear resistance. Although a substantial oxida-  
tion peak occurred about 0.4 mm below the surface, because  
of the very high wear resistance of the 28 Mrad cups, the  
total penetration due to wear was too shallow to reach this  
sub-surface oxidized zone, even after 4 million cycles.

For the non-remelted 3.3 Mrad cups, subsurface oxidation, peaking at about 1 mm below the surface (Fig. 14), occurred after aging in air at 80 °C for 20 days. Since the total depth of penetration of these cups was about 300 microns (at 7 million cycles), the full effect of this subsurface oxidation would not become apparent until a much larger number of wear cycles.

Nevertheless, the sub-surface oxidation in the non-remelted cups (EXAMPLE 3, particularly for the 28 Mrad specimen) leads to reduced molecular weight, a reduction in crosslinking (as indicated by gel content) and an increased crystallinity and brittleness, all of which can contribute to reductions in mechanical properties such as fatigue strength and, eventually, a reduction in wear resistance. Although remelting had no apparent effect on the wear resistance of the aged cups in the present example, the elimination of free radicals by remelting improves the long-term resistance to oxidation, thereby improving the long-term wear resistance *in vivo*.

#### EXAMPLE 5: WEAR TESTING OF GAMMA-IRRADIATED UHMWPE WITH MULTIPLE DOSES

##### Materials and Methods

In EXAMPLE 2, we demonstrated the improved wear resistance of UHMWPE acetabular cups that resulted from exposure to 28 Mrad gamma radiation, as compared to cups irradiated to 3.3 Mrad. The average wear rate of the 28 Mrad cups was less than 2% of that of the 3.3 Mrad cups (i.e., a dose within the normal 2.5 to 4.0 Mrad range used to sterilize implants). To examine the wear as a function of radiation dose and, thereby, determine an optimum dose for reducing wear, extruded bars of GUR 4150 UHMWPE, 3" diameter x 15" long, were gamma irradiated in air, three bars at each dose of 4.5, 9.5, 14.5, 20.2 or 24 Mrad (SteriGenics, Inc.,

Corona, CA), at a dose rate of 0.45 Mrad/hour. Additional  
20 bars were irradiated in air to 50 or 100 Mrad (SteriGenics  
Inc., Tustin, CA), at a dose rate of 0.67 Mrad/hour. For  
each radiation dose, two bars were then remelted by heating  
in an oven in ambient atmosphere from room temperature to  
150 °C at about 0.3 °C/min, holding at 150 °C for 5 hours  
25 and then slowly-cooled to room temperature, with the third  
bar not being remelted. The irradiated-remelted bars were  
used to produce acetabular cups for the wear tests.

Seven sets of acetabular cups were machined from the  
irradiated-remelted bars for each of the seven doses at a  
30 commercial machining shop (Bradford and Meneghini Manufac-  
turing Co., Santa Fe Springs, CA). Each cup had a 2" O.D.  
and 1.26" I.D., with 1" outer radius and 0.63" inner radius  
(Fig. 6). Wear tests were run on the remelted specimens,  
using two cups for each radiation dose from 4.5 to 24 Mrad,  
35 and one cup each for 50 and 100 Mrad. The bars were inten-  
tionally used with larger diameters than the final cups so  
that the process of machining away the outer layer of each  
bar, about 0.5 inch thick, effectively removed the most  
oxidized, most crystalline, least crosslinked surface layer  
40 (about 0.5 to 1.0 mm). In this manner the bearing surface of  
each cup consisted of material from near the center of the  
bar, i.e., the most crosslinked, least crystalline, least  
oxidized region, which was expected to be the most wear  
resistant.

45 Because acetabular cups used in patients must first be  
sterilized by some acceptable means, the test cups in this  
study were sterilized prior to wear testing using ethylene  
oxide at the appropriate dose for clinical implants. Ethyl-  
ene oxide was chosen instead of additional gamma irradiation  
50 (e.g., 2.5-4.0 Mrad) in order to focus the results on the  
effects of the radiation doses used to crosslink the materi-  
als. Prior to wear testing, the cups were pre-soaked in  
distilled water for four weeks to minimize additional fluid

absorption during the wear test, thereby making the weight  
loss method for wear measurement more accurate. The details  
for the wear test method were described in EXAMPLE 2.

### Results

Fig. 21 shows the soak-corrected wear (volume loss) of  
each material (three cups for 3.3 Mrad from EXAMPLE 2, two  
cups each for radiation dose from 4.5 to 24.5 Mrad, and one  
cup each for 50 and 100 Mrad). The individual wear rates,  
determined by linear regression, and the mean values for  
each type of material are listed in Table 5. At about 2.1  
million cycles, there was a temporary overloading of the  
test cups, due to a malfunction of the computer controller.  
Although this overload had only a minor effect on the wear  
rates of the cups, the cup irradiated to 100 Mrad cracked  
and was, therefore, removed from the test.

Fig. 22 shows the average wear rate (volume loss from 1  
to 5 million) of each type of material, that had been re-  
melted (denoted in the figure by darkened circles) and that  
had not been re-melted (denoted in the figure by an open  
circle), as a function of dose.

The wear of the cups subjected to 3.3 or 4.5 Mrad with  
remelting averaged 17.5 or 9.3 mm<sup>3</sup> per million cycles,  
respectively, showing about 13% or 54% lower wear than for  
the 3.3 Mrad non-remelted cups (20.1 mm<sup>3</sup> per million cy-  
cles). In contrast, the wear rate of the 9.5 Mrad remelted  
cups averaged 2.2 mm<sup>3</sup> per million cycles, i.e., about 89%  
lower than for the 3.3 Mrad non-remelted cups. For radiation  
doses greater than 9.5 Mrad, minimal systematic wear oc-  
curred, such that, compared to that with 3.3 Mrad non-re-  
melted cups, the wear rates were about 94% lower for the  
14.5 Mrad remelted cups, and minimal wear (>99% reduction)  
for the 20.2 Mrad remelted cups.

"Negative" wear rates were calculated for the cups  
given 24 Mrad or greater doses. Apparently, these cups

absorbed more water than the soak control cups, and the error between the two was greater than the weight loss due to wear, giving a net gain in weight.

### Discussion

The results clearly demonstrated that the wear resistance of UHMWPE acetabular cups were improved substantially with increasing radiation dose over the range of 4.5 to 9.5 Mrad (i.e., with increasing crosslinking), such that wear was too small to accurately quantify for doses exceeding about 20 Mrad. Since, in addition to improving wear resistance, radiation induced crosslinking may degrade other physical properties, such as elongation to failure and fatigue strength, the dose-response curve developed in the present example provides the opportunity to select an optimum dose, i.e., one that provides the desired amount of improvement in wear resistance with a minimum reduction in other physical properties. The procedure for arriving at the choice of dose for a particular *in vivo* application is described in this application.

UHMWPE acetabular cups that had been compression molded and then exposed to 3.1 Mrad gamma radiation in air but were not thermally treated (i.e., typical of commercially used implants over the past two decades), showed an approximate wear rate of 33.1 mm<sup>3</sup>/million cycle using the procedure of the wear test described in EXAMPLE 2, above. When compared to these conventional UHMWPE acetabular cups, the acetabular cups of the present invention (i.e., irradiated bar stock, remelted and machined into cups) show the following percentage reduction in wear rate: for the 3.3 Mrad remelted acetabular cup from EXAMPLE 2, above (about 47% reduction in wear rate); 4.5 Mrad remelted acetabular cup from EXAMPLE 5, above (about 72% reduction in wear rate); 9.5 Mrad remelted acetabular cup from EXAMPLE 5, above (about 93% reduction in wear rate).



EXAMPLE 6: PHYSICAL CHARACTERIZATION OF GAMMA-IRRADIATED  
UHMWPE WITH OR WITHOUT REMELTING

Materials and Methods

The materials for physical characterization were the same as the wear tested materials described in EXAMPLE 5.

The materials included UHMWPE extruded bars (3" in diameter) gamma irradiated to 3.3, 4.5, 9.5, 14.5, 20.2, 24, 50 and 100 Mrad, with or without remelting, and the non-irradiated bars. 8 mm thick disks were cut out of irradiated bars with or without remelting, and sterilized with ethylene oxide.

The specimens for DSC and swelling measurements were cut out of the center of the 8 mm thick disks. The DSC measurement for crystallinity and melting temperature with sample weighing about 4 mg was described in EXAMPLE 1. For swelling measurements, 1 mm thick sheet weighing about 0.5 gram was cut out of the center of the 8 mm thick disk, and extraction of the sol-fraction was performed in boiling p-xylene for 72 hours, with 0.5 wt % antioxidant (2,6-di-t-butyl-4-methyl phenol) being added to prevent oxidation. After extraction, the gel was transferred to fresh p-xylene and allowed to equilibrate at 120°C for 2 hours. The swollen gel was then quickly transferred to a weighing bottle, covered and weighed. The data was obtained as the average of five measurements. After measurements, samples were deswollen in acetone and then dried at 60°C in a vacuum oven to a constant weight. The gel fraction was determined as the ratio of the weight of the dried extracted to the initial dry non-extracted network. The degree of swelling was calculated as the ratio of the weight of the swollen gel to the dried extracted gel. The degree of swelling was used to calculate the network chain density, number-average molecular weight between crosslinks and crosslink density, according to the theory of Flory and Rehner {Shen et al., J. Polym. Sci., Polym. Phys., 34:1063-1077 (1996)}. For examining the

oxidation profiles of the extruded bars irradiated and remelted in air, a two hundred micron thick section was microtomed perpendicular to the bar surface and examined by FTIR as a function of depth from the bar surface.

### Results and Discussion

The melting temperature and crystallinity for non-irradiated, and irradiated (with and without remelting) materials are shown in Table 6. The degree of swelling, average molecular weight between crosslinks, crosslink density and gel content are shown in Table 7. After irradiation, the melting temperature and crystallinity increased, ranging from 135.3 to 140.2°C, and about 60 to 71%, respectively, over the dose range studied. Remelting of the irradiated bars resulted in reductions in the melting temperature and crystallinity, ranging from about 131 to 135°C, and about 51 to 53%, respectively.

As shown in Table 7, with increasing radiation dose, the degree of swelling and average molecular weight between crosslinks decreased, while the crosslink density increased. The gel content, in general, increased with radiation dose, but reached a plateau region at about 9.5 Mrad. With remelting, the degree of swelling and average molecular weight between crosslinks for bars irradiated up to 9.5 Mrad were significantly reduced, but remained almost unchanged after 9.5 Mrad. The crosslink density increased, after remelting, with dose up to 9.5 Mrad and then remained almost unchanged. The gel content, generally, increased after remelting.

The oxidation profiles for the 9.5 and 24 Mrad materials, after remelting at 150°C in air for 5 hours, as a function of depth from the bar surface are shown in Fig. 24. The results clearly showed that the oxidation drops tremendously within 1 mm, and the most oxidized layer is about 1 mm deep below the surface, after irradiation and remelting in air.

EXAMPLE 7: TENSILE PROPERTIES OF GAMMA-IRRADIATED UHMWPE AT  
VARIOUS DOSES, WITH OR WITHOUT REMELTING

Materials and Methods

The materials for tensile test are the same as the wear tested materials described in EXAMPLE 5, above. The materials included UHMWPE extruded bars (3" in diameter) gamma irradiated to 4.5, 9.5, 14.5, 20.2, and 24 Mrad, with or without remelting, and non-irradiated bars. Five tensile specimens each was machined out of the center of the 3" diameter bars according to ASTM F648-96 and D-638 (type IV). Tensile tests were performed using an servo-hydraulic tensile test machine at speed of 2 inches/min.

Results and Discussion

The tensile strength at yield, elongation, and tensile strength (ultimate) at breaks are shown in Table 8. The average tensile properties as a function of radiation dose are shown in Figs. 25-27. The tensile strength at yield after irradiation was higher than that of non-irradiated material, and slightly increased with radiation dose. Remelting of the irradiated bars resulted in a reduction in tensile strength at yield, and the strength remained almost constant over the dose range studied (Fig. 25). The tensile strength (ultimate) and elongation at break decreased with increasing doses (Figs. 26-27). Remelting resulted in further reduction in ultimate tensile strength over the dose range. However, remelting had almost no effect on the elongation at break over the same dose range.

All publications and patent applications mentioned in this Specification are herein incorporated by reference to the same extent as if each of them had been individually indicated to be incorporated by reference.

20        Although the foregoing invention has been described in  
some detail by way of illustration and example for purposes  
of clarity and understanding, it will be obvious that vari-  
ous modifications and changes which are within the skill of  
those skilled in the art are considered to fall within the  
scope of the appended claims. Future technological advance-  
25        ments which allows for obvious changes in the basic inven-  
tion herein are also within the claims.

Table 1 3.3 Mrad

| Distance<br>from surface<br>( mm ) | Before remelting                      |                                     |                      | After remelting                       |                                     |                      |
|------------------------------------|---------------------------------------|-------------------------------------|----------------------|---------------------------------------|-------------------------------------|----------------------|
|                                    | peak melting<br>temperature<br>( °C ) | degree of<br>crystallinity<br>( % ) | gel content<br>( % ) | peak melting<br>temperature<br>( °C ) | degree of<br>crystallinity<br>( % ) | gel content<br>( % ) |
| 34.8 - 35                          | 135.3                                 | 59.6                                | 91                   | 131.4                                 | 52.5                                | 94.7                 |
| 35.8 - 36                          | 135.4                                 | 60.2                                | 91                   | 131.5                                 | 51.2                                | 94.7                 |
| 36.8 - 37                          | 135.3                                 | 60.5                                | 91                   | 131.4                                 | 51.9                                | 94.7                 |
| 37.8 - 38<br>(center)              | 135.3                                 | 60                                  | 91.1                 | 131.3                                 | 52                                  | 95                   |

Table 2 28 Mrad

| Distance<br>from surface<br>( mm ) | Before remelting                      |                                     |                      | After remelting                       |                                     |                      |
|------------------------------------|---------------------------------------|-------------------------------------|----------------------|---------------------------------------|-------------------------------------|----------------------|
|                                    | peak melting<br>temperature<br>( °C ) | degree of<br>crystallinity<br>( % ) | gel content<br>( % ) | peak melting<br>temperature<br>( °C ) | degree of<br>crystallinity<br>( % ) | gel content<br>( % ) |
| 34.8 - 35                          | 139.8                                 | 65.1                                | 95.8                 | 135                                   | 52                                  | 97.7                 |
| 35.8 - 36                          | 139.8                                 | 64.2                                | 95.8                 | 134.8                                 | 52.1                                | 97.7                 |
| 36.8 - 37                          | 139.7                                 | 64.5                                | 95.8                 | 134.9                                 | 52.5                                | 97.7                 |
| 37.8 - 38<br>(center)              | 139.7                                 | 65.3                                | 95.8                 | 134.9                                 | 52.7                                | 97.7                 |

Table 3

| Cup # | Material                    | Wear Rate<br>(mm <sup>3</sup> /million<br>cycles) | Mean Wear<br>Rate $\pm$ Std<br>Deviation |
|-------|-----------------------------|---|--|
| N11   | 3.3 Mrad<br>Not<br>remelted | 20.8  | 21.1 $\pm$ 0.3                           |
| N16   |                             | 21.2  |  |
| N17   |                             | 21.4  |  |
| R21   | 3.3 Mrad<br>Remelted        | 17.7  | 18.6 $\pm$ 1.3                           |
| R26   |                             | 20.1  |  |
| R27   |                             | 18.0  |  |
| N35   | 28 Mrad<br>Not<br>remelted  | 0.29  | 0.25 $\pm$ 0.03                          |
| N31   |                             | 0.24  |  |
| N32   |                             | 0.24  |  |
| R48   | 28 Mrad<br>Remelted         | 0.36  | 0.36 $\pm$ 0.001                         |
| R45   |                             | 0.35  |  |
| R49   |                             | 0.36  |  |

Table 4

| Cup # | Material | 0 - 3 Million Cycles<br>(non- aged)               |  | 3 - 7 Million Cycles |   |  |
|-------|----------|---|--|----------------------|---|--|
|       |          | Wear Rate<br>(mm <sup>3</sup> /million<br>cycles) | Mean Wear<br>Rate $\pm$ Std<br>Deviation | Conditions           | Wear Rate<br>(mm <sup>3</sup> /million<br>cycles) | Mean Wear<br>Rate $\pm$ Std<br>Deviation |
| N11   | 3.3 Mrad | 20.8  | 21.1 $\pm$ 0.3                           | non-aged             | 21.2  | -  |
| N16   | Not      | 21.2  |  | aged                 | 21.5  | 21.8 $\pm$ 0.5                           |
| N17   | remelted | 21.4  |  | aged                 | 22.2  |  |
| R21   | 3.3 Mrad | 17.7  | 18.6 $\pm$ 1.3                           | non-aged             | 17.5  | -  |
| R26   | Remelted | 20.1  |  | aged                 | 19.2  | 19.8 $\pm$ 1.0                           |
| R27   |          | 18.0  |  | aged                 | 20.5  |  |
| N35   | 28 Mrad  | 0.29  | 0.25 $\pm$ 0.03                          | non-aged             | 0.03  | -  |
| N31   | Not      | 0.24  |  | aged                 | - 0.47  | - 0.71 $\pm$ 0.3                         |
| N32   | remelted | 0.24  |  | aged                 | - 0.93  |  |
| R48   | 28 Mrad  | 0.36  | 0.36 $\pm$ 0.001                         | non-aged             | 0.47  | -  |
| R45   | Remelted | 0.35  |  | aged                 | 0.08  | - 0.06 $\pm$ 0.2                         |
| R49   |          | 0.36  |  | aged                 | - 0.20  |  |

Table 5 (1 - 5 million cycles)

| Cup # | Material                    | Wear Rate<br>(mm <sup>3</sup> /million cycles) | Mean Wear Rate $\pm$ SD<br>(mm <sup>3</sup> /million cycles) |
|-------|-----------------------------|--|--|
| N11   | 3.3 Mrad<br>Not<br>remelted | 20.46  | 20.12 $\pm$ 0.7 *  |
| N16   |                             | 19.32  |  |
| N17   |                             | 20.59  |  |
| R21   | 3.3 Mrad Remelted           | 17.04  | 17.51 $\pm$ 0.48 *   |
| R26   |                             | 18.0   |  |
| R27   |                             | 17.49  |  |
| RA2   | 4.5 Mrad Remelted           | 9.93   | 9.28 $\pm$ 0.92  |
| RA3   |                             | 8.63   |  |
| RB3   | 9.5 Mrad Remelted           | 2.39   | 2.22 $\pm$ 0.24  |
| RB6   |                             | 2.05   |  |
| RC5   | 14.5 Mrad Remelted          | 1.26   | 1.17 $\pm$ 0.13  |
| RC6   |                             | 1.08   |  |
| RD1   | 20.2 Mrad Remelted          | 0.26   | 0.12 $\pm$ 0.2   |
| RD6   |                             | -0.02  |  |
| RE3   | 24 Mrad Remelted            | -0.49  | -0.59 $\pm$ 0.13   |
| RE4   |                             | -0.68  |  |
| RF2   | 50 Mrad Remelted            | -0.8   | -  |
| RG1   | 100 Mrad Remelted           | -6.88**  | -  |

\*The wear data of the 3.3 Mrad materials in Example 2.

\*\*The wear rate in the period of 1 - 2 million cycles.



Table 6

| Samples    | Non-remelted          |                      | Remelted              |                      |
|------------|-----------------------|----------------------|-----------------------|----------------------|
|            | Melting point<br>(°C) | Crystallinity<br>(%) | Melting point<br>(°C) | Crystallinity<br>(%) |
| Non-irrad. | 133.8                 | 55                   | -                     | -                    |
| 3.3 Mrad   | 135.3 ± 0.1           | 60.1 ± 0.4           | 131.4 ± 0.1           | 51.8 ± 0.6           |
| 4.5 Mrad   | 136.2 ± 0.2           | 65.8 ± 1.6           | 131.6 ± 0.2           | 52.0 ± 1.3           |
| 9.5 Mrad   | 137.1 ± 0             | 67.1 ± 2.2           | 134.8 ± 0.2           | 53.3 ± 2.1           |
| 14.5 Mrad  | 137.5 ± 0.2           | 69.6 ± 1.6           | 135.0 ± 0.1           | 53.0 ± 1.5           |
| 20.2 Mrad  | 137.4 ± 0.1           | 70.8 ± 2.8           | 135.3 ± 0.1           | 52.1 ± 1.8           |
| 24 Mrad    | 137.9 ± 0.3           | 68.0 ± 1.3           | 135.2 ± 0.1           | 51.7 ± 1.2           |
| 50 Mrad    | 138.9 ± 0.2           | 67.0 ± 1.3           | 135.2 ± 0             | 52.8 ± 0.2           |
| 100 Mrad   | 140.2 ± 0.3           | 66.3 ± 2.7           | 130.8 ± 0.2           | 52.3 ± 1.7           |

Table 7

| Samples   | Non- remelted      |                                 |                          |                 | Remelted           |                                 |                          |                 |
|-----------|--------------------|---------------------------------|--------------------------|-----------------|--------------------|---------------------------------|--------------------------|-----------------|
|           | Degree of swelling | M.W. between crosslinks (g/mol) | Crosslink density (mol%) | Gel content (%) | Degree of swelling | M.W. between crosslinks (g/mol) | Crosslink density (mol%) | Gel content (%) |
| 3.3 Mrad  | 5.29               | 8400                            | 0.17                     | 94.7            | 3.21               | 2500                            | 0.56                     | 98.1            |
| 4.5 Mrad  | 3.57               | 3500                            | 0.40                     | 97.8            | 3.15               | 2400                            | 0.58                     | 98.4            |
| 9.5 Mrad  | 2.82               | 1900                            | 0.74                     | 98.6            | 2.54               | 1400                            | 1.0                      | 98.9            |
| 14.5 Mrad | 2.35               | 1100                            | 1.27                     | 98.7            | 2.36               | 1100                            | 1.27                     | 99.2            |
| 20.2 Mrad | 2.27               | 1000                            | 1.40                     | 98.8            | 2.25               | 1000                            | 1.40                     | 99.2            |
| 24 Mrad   | 2.17               | 900                             | 1.56                     | 98.7            | 2.24               | 1000                            | 1.40                     | 99.2            |
| 50 Mrad   | 1.92               | 600                             | 2.33                     | 98.7            | 2.17               | 900                             | 1.56                     | 99.1            |
| 100 Mrad  | 1.71               | 400                             | 3.50                     | 98.6            | 1.71               | 400                             | 3.50                     | 98.5            |

Table 8

| Materials                | Tensile Strength at<br>Yield (MPa) | Tensile Strength at<br>Break (MPa) | Elongation at<br>Break (%) |
|--------------------------|------------------------------------|------------------------------------|----------------------------|
| Non-irradiated           | $23.3 \pm 0.11$                    | $52.1 \pm 4.78$                    | $356 \pm 23$               |
| <b>Without remelting</b> |                                    |                                    |                            |
| 4.5 Mrad                 | $24.9 \pm 0.33$                    | $46.9 \pm 2.91$                    | $314 \pm 12$               |
| 9.5 Mrad                 | $25.3 \pm 0.12$                    | $47.6 \pm 2.76$                    | $251 \pm 8$                |
| 14.5 Mrad                | $25.7 \pm 0.25$                    | $46.4 \pm 1.20$                    | $213 \pm 5$                |
| 20.2 Mrad                | $26.2 \pm 0.27$                    | $40.2 \pm 2.72$                    | $175 \pm 7$                |
| 24 Mrad                  | $26.4 \pm 0.23$                    | $40.0 \pm 5.42$                    | $164 \pm 17$               |
| <b>After remelting</b>   |                                    |                                    |                            |
| 4.5 Mrad                 | $21.5 \pm 0.33$                    | $45.6 \pm 8.89$                    | $309 \pm 20$               |
| 9.5 Mrad                 | $21.3 \pm 0.60$                    | $43.2 \pm 2.80$                    | $252 \pm 8$                |
| 14.5 Mrad                | $21.8 \pm 0.29$                    | $36.8 \pm 1.72$                    | $206 \pm 9$                |
| 20.2 Mrad                | $21.9 \pm 0.18$                    | $34.3 \pm 3.61$                    | $185 \pm 8$                |
| 24 Mrad                  | $21.7 \pm 0.25$                    | $32.3 \pm 2.81$                    | $160 \pm 19$               |

We claim:

20

1. A preformed polymeric composition comprising a crosslinked thermally treated polymer.

25

2. The composition of claim 1, wherein the composition possesses one or more of the following characteristics: degree of swelling of between about 1.7 to about 5.3; molecular weight between crosslinks of between about 400 to about 8400 g/mol; and a gel content of between about 95 to about 99 %.

30

3. The composition of claim 1, wherein the preformed polymeric composition is crosslinked by gamma radiation at a dose from about 1 to about 100 Mrad.

35

4. The composition of claim 3, wherein the dose is from about 5 to about 25 Mrad.

5. An *in vivo* implant comprising a crosslinked and remelted polymer.

40

6. A method for increasing the wear resistance of a preformed polymeric composition, comprising the steps of:

(a) crosslinking the polymeric composition in a solid state; and

45

(b) subjecting the crosslinked polymeric composition to thermal treatment.

50

7. The method of claim 6, further comprising the step of removing the most oxidized surface of the thermally treated crosslinked polymeric composition.

8. The method of claim 6, wherein the crosslinking is by gamma irradiation.

20 9. The method of claim 8, wherein the gamma irradiation is at a dose of from about 1 to about 100 Mrad.

10. The method of claim 6, wherein the thermal treatment comprises remelting the crosslinked polymer.

25 11. The method of claim 10, wherein the remelting temperature is between the melting temperature of the irradiated polymer to about 160°C above the melting temperature of the irradiated polymer.

30 12. The method of claim 6, wherein the resulting polymeric composition possesses one or more of the following characteristics: degree of swelling of between about 1.7 to about 5.3; molecular weight between crosslinks of between about 400 to about 8400 g/mol; and a gel content of between  
35 about 95 to about 99 %.

13. The method of claim 6, wherein the thermal treatment comprises annealing the crosslinked polymer.

40 14. The method of claim 13, wherein the annealing temperature is from about 90°C below to about 1°C below the melting temperature of the irradiated polymer.

15. A polymeric composition made from the steps of:  
45 (a) crosslinking a starting polymer in a solid state to form a crosslinked polymer; and  
(b) subjecting the crosslinked polymer to thermal treatment.

50 16. The polymeric composition of claim 15, further comprising the step of removing the most oxidized surface of the crosslinked polymeric composition.

20 17. The polymeric composition of claim 15, wherein the crosslinking is by gamma irradiation.

25 18. The polymeric composition of claim 17, wherein the gamma irradiation is at a dose of from about 1 to about 100 Mrad.

19. The polymeric composition of claim 15, wherein the thermal treatment comprises remelting the crosslinked polymer.

30 20. The polymeric composition of claim 19, wherein the remelting temperature is between the melting temperature of the irradiated polymer to about 160°C above the melting temperature of the irradiated polymer.

35 21. The polymeric composition of claim 15, wherein the thermal treatment comprises annealing the crosslinked polymer.

40 22. The method of claim 21, wherein the annealing temperature is between about 90°C below to about 1°C below the melting temperature of the irradiated polymer.

23. A product made by the process of:

45 (a) crosslinking a preformed polymeric composition in a solid state;

(b) subjecting the crosslinked polymeric composition to thermal treatment; and

(c) fashioning the product from the crosslinked polymeric composition.

50

24. The product of claim 23, further comprising the step of removing the most oxidized surface of the crosslinked polymer.

20        25. The product of claim 24, wherein the product is an  
in vivo implant.

25        26. A method for determining an optimal radiation dose  
and thermal treatment for treating a polymer to increase its  
wear resistance, when made into a desired product, while  
maintaining its desirable physical and/or chemical proper-  
ties, the method comprises the steps of:

      (a) irradiating the polymer in the solid state over a  
range of radiation doses likely to produce the desirable  
wear resistance and physical and/or chemical properties;

30        (b) remelting the polymer;

      (c) correlating the radiation doses with the wear rate  
of the desired product made from the irradiated remelted  
polymer using actual or simulated wear conditions for the  
desired product;

35        (d) correlating the radiation doses with each of the  
physical and/or chemical properties of the desired product  
made from the irradiated remelted polymer using actual or  
simulated wear conditions for the desired product;

40        (e) comparing the correlations in steps (c) and (d) to  
determine the optimal radiation dose which will produce a  
desirable wear rate while maintaining the desirable physical  
and/or chemical properties, if such a radiation dose is  
arrived at, use this optimal radiation dose for future  
treatment of the polymer;

45        (f) if the optimal radiation dose cannot be arrived at  
in step (e), then determining a dose that would produce a  
desirable wear rate based on the correlation of step (c) and  
annealing instead of remelting the polymer which has been  
irradiated to said dose;

50        (g) correlating the physical and/or chemical proper-  
ties of the desired product made from the irradiated and  
annealed polymer, using actual or simulated wear conditions

for the desired product, with different annealing times and  
20 temperatures;

(h) determining an annealing temperature and time  
which will provide the desirable wear rate and physical  
and/or chemical properties, if this is possible, then use  
the radiation dose and annealing conditions determined at  
25 this step for future treatment of the polymer;

(i) if step (h) does not provide the desirable wear  
rate and physical and/or chemical properties, then apply a  
lower radiation dose and repeat steps (c) to (i) or (h)  
until the optimal radiation dose and annealing conditions  
30 are determined or the steps confirm that no optimal radia-  
tion dose and annealing conditions can be obtained for the  
desired wear rate and physical and/or chemical properties.

27. The method of claim 26, wherein the irradiation is  
35 gamma irradiation between a range of about 1 to 100 Mrad;  
the remelting temperature is between the melting temperature  
of the irradiated polymer to about 160°C above the melting  
temperature of the irradiated polymer; and the annealing  
temperature is between about 90°C below to about 1°C below  
40 the melting temperature of the irradiated polymer.

28. A polymer produced by irradiation and thermal  
treatment, wherein the radiation dose and remelting or  
annealing conditions are determinable by the method of claim  
45 27.

29. An in vivo implant made from the polymer of claim  
26, wherein the most oxidized surface of the polymer is  
removed.

50 30. A process for treating a polymer, wherein the  
process employs radiation dose and remelting or annealing  
conditions determinable by the steps of claim 26.



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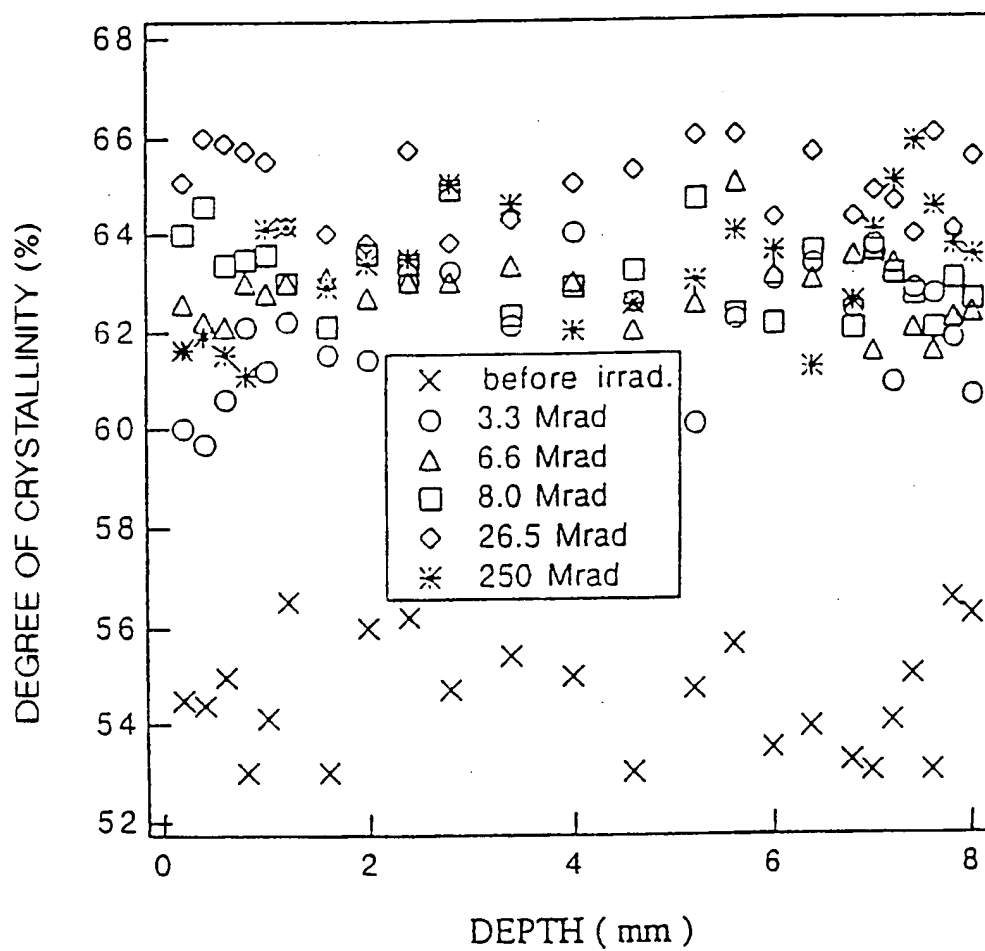


FIG. 1

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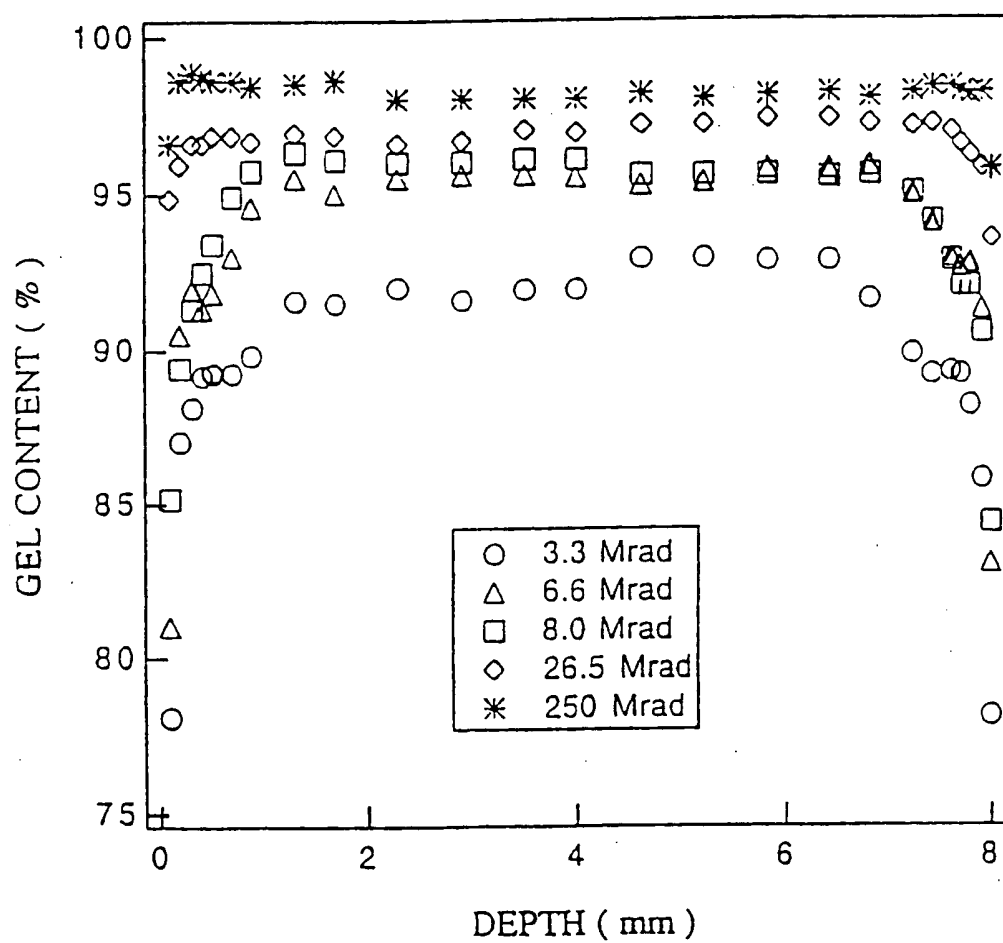


FIG. 2

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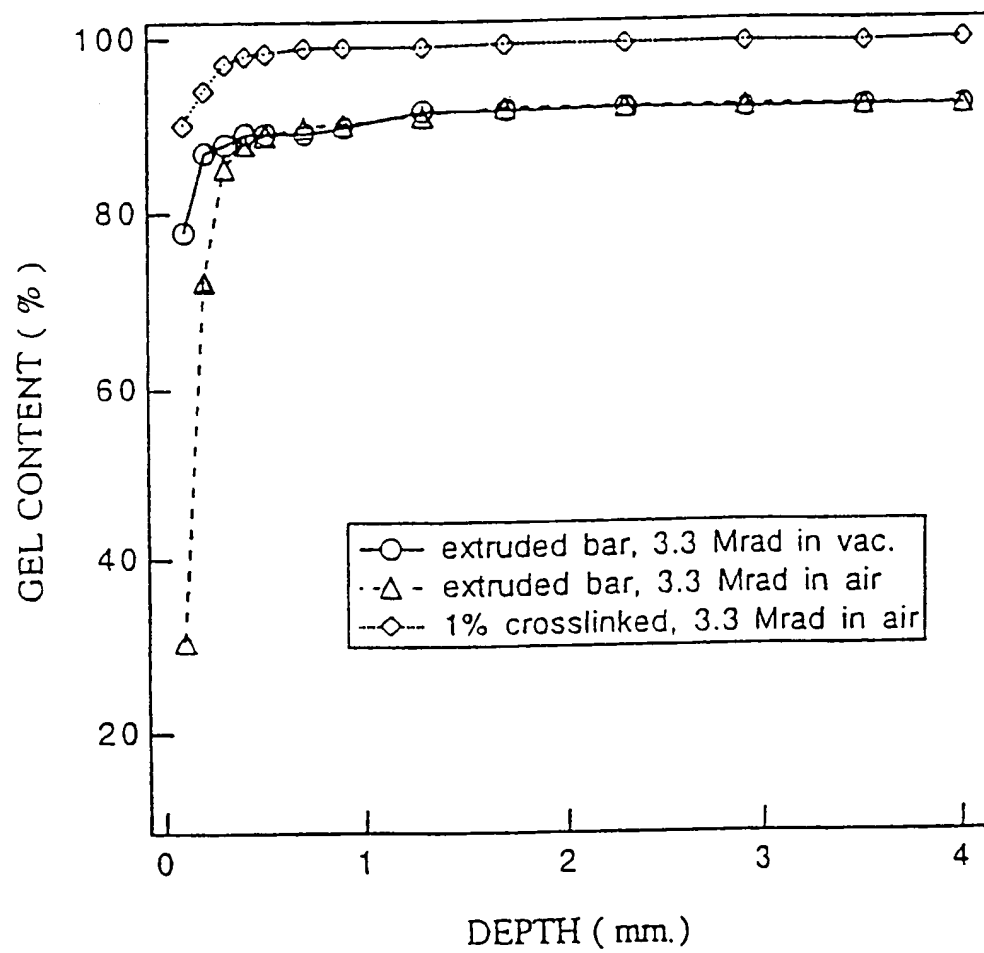


FIG. 3

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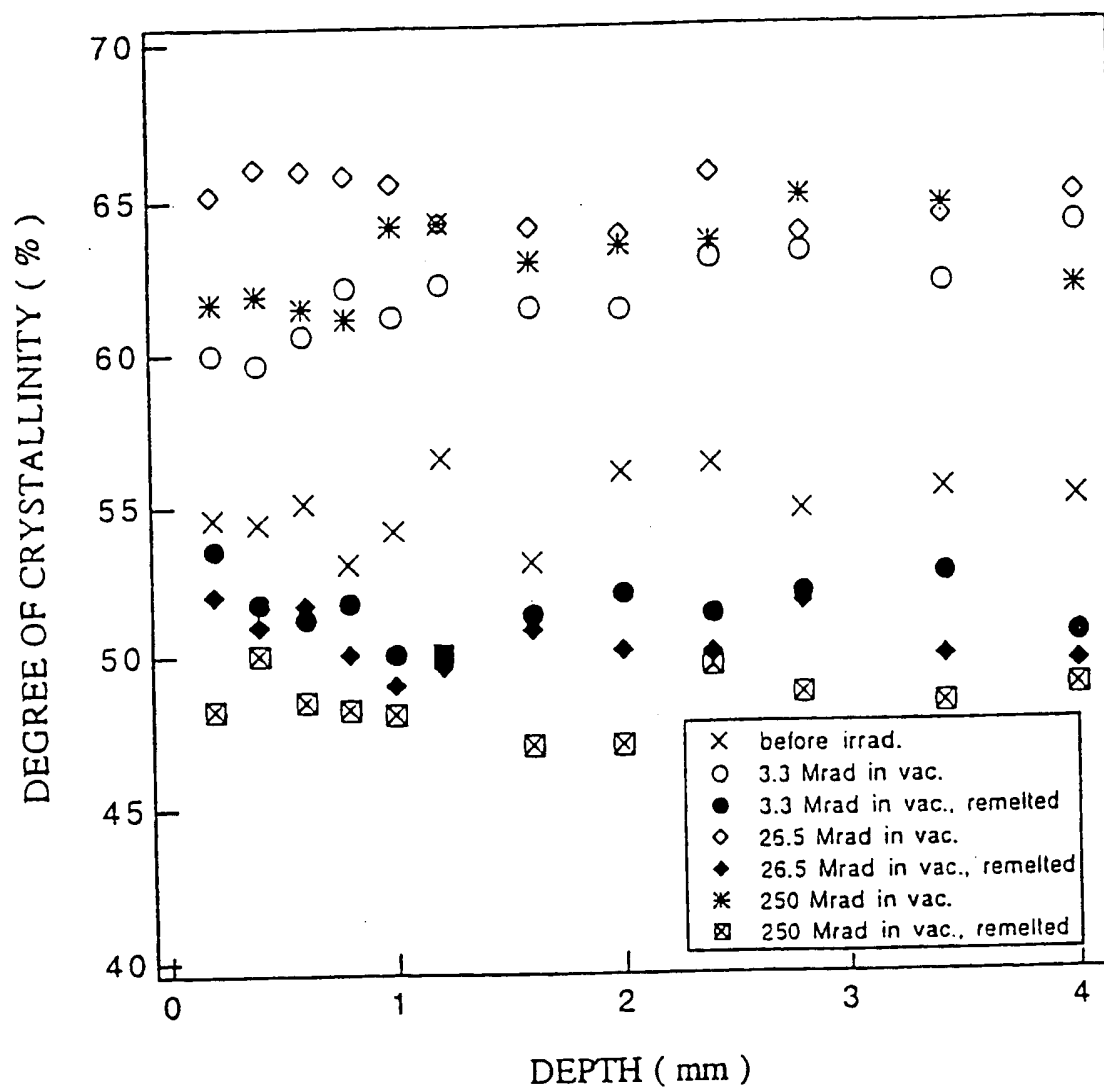


FIG. 4

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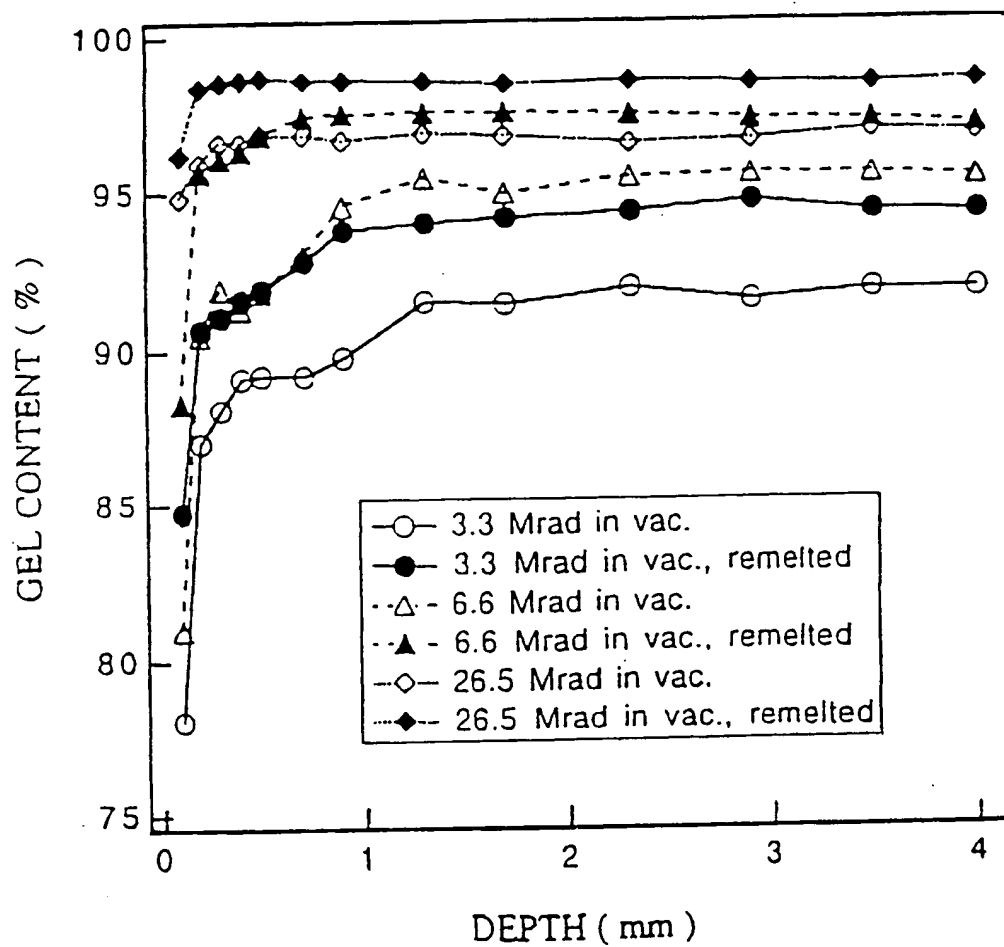
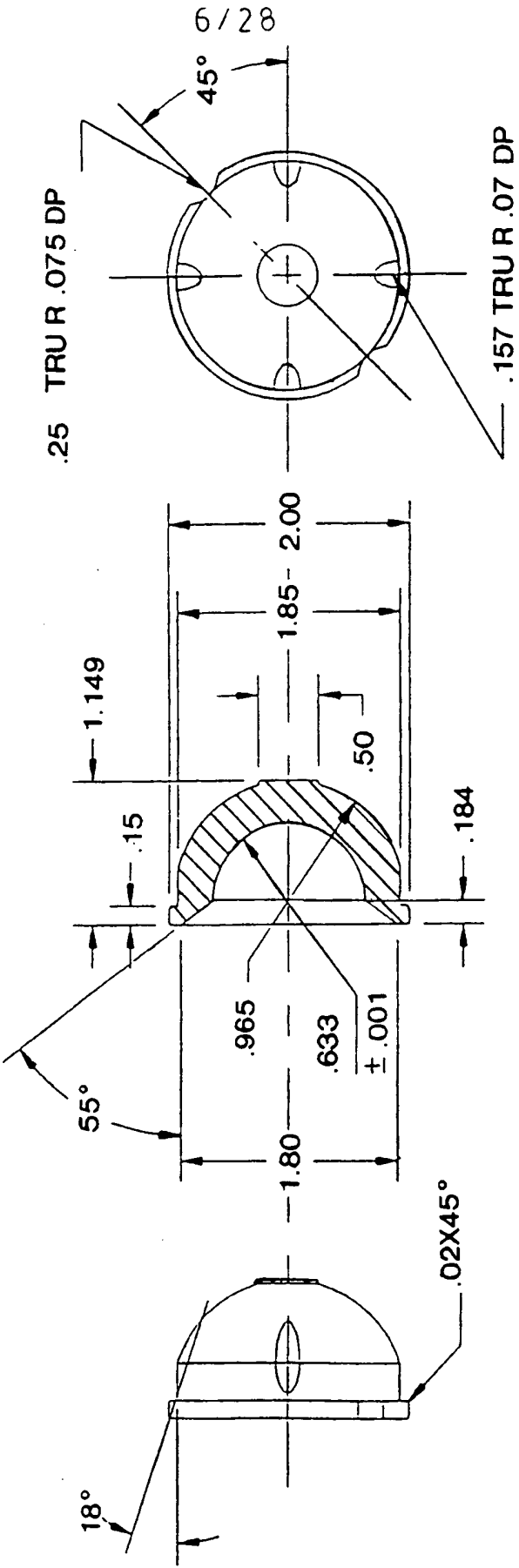


FIG. 5

FIG. 6



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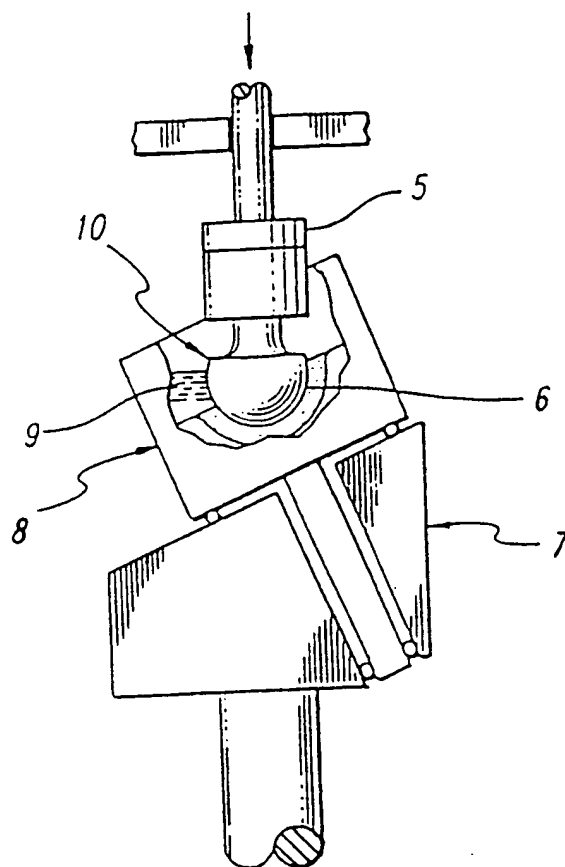


FIG. 7

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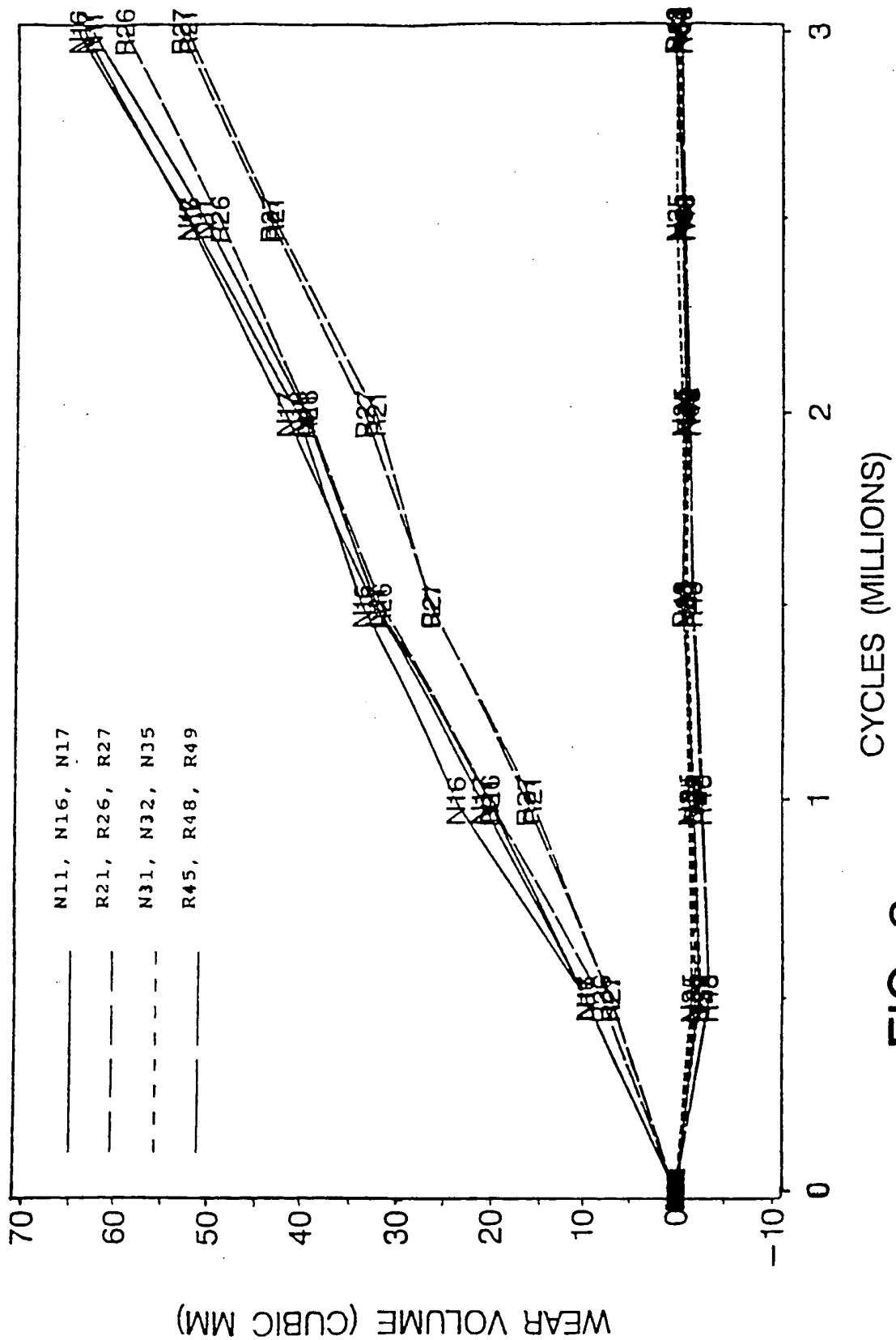


FIG. 8



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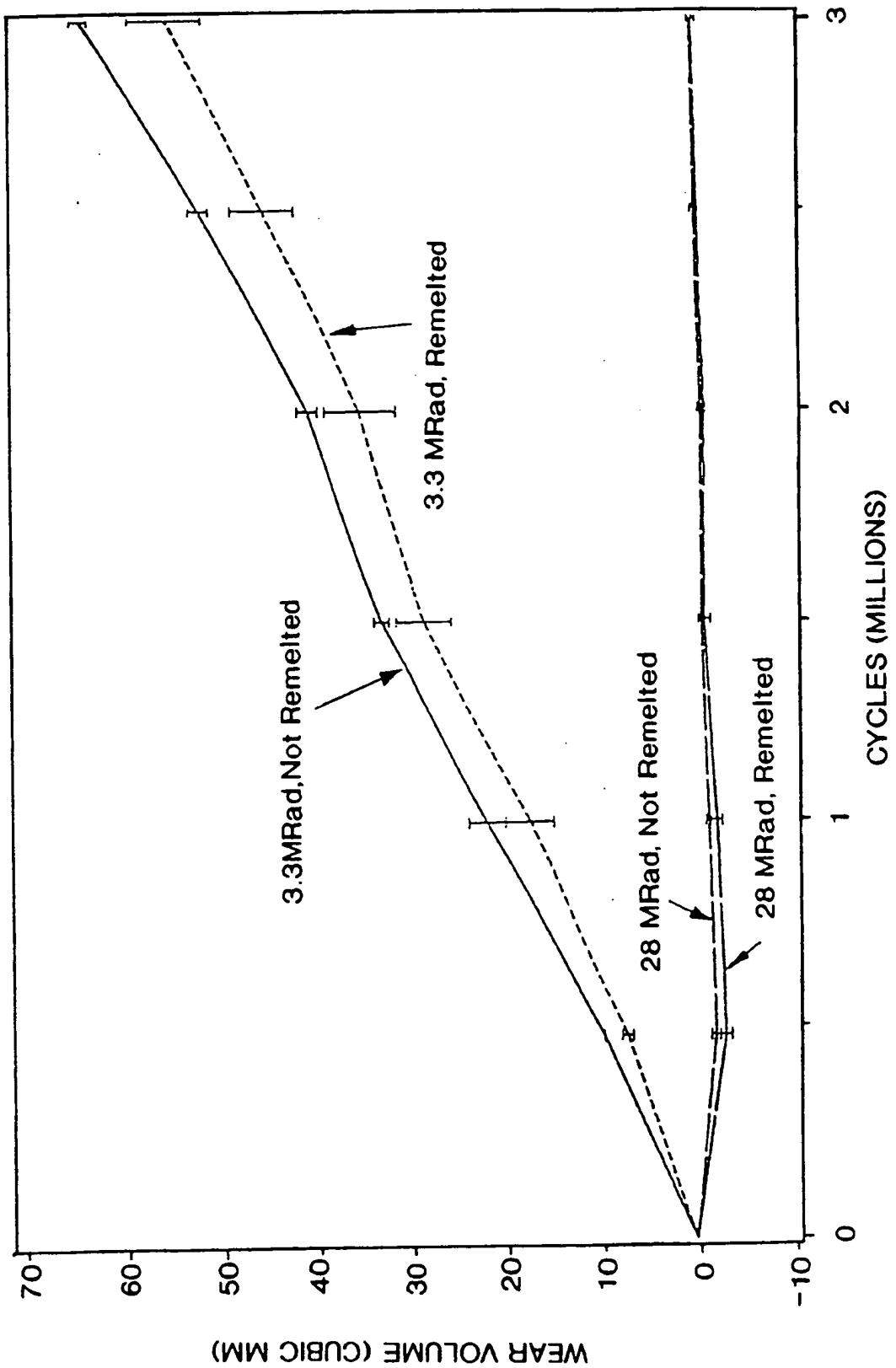


FIG. 9

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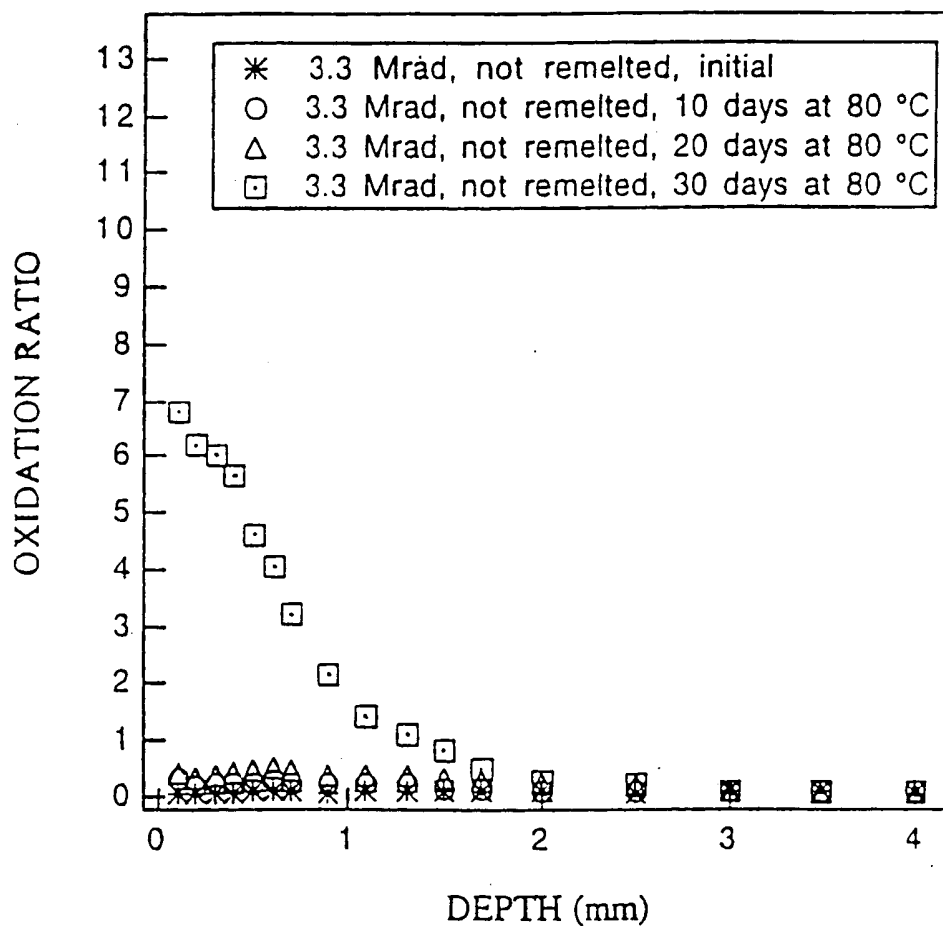


FIG. 10

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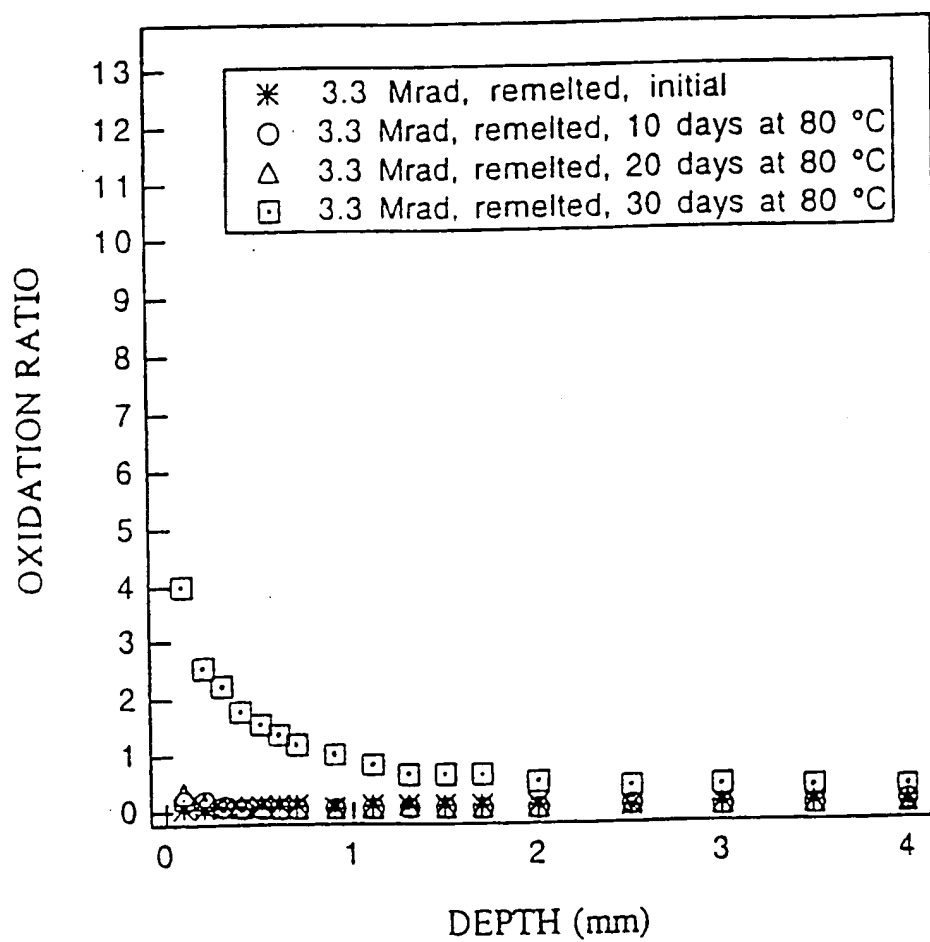


FIG. 11

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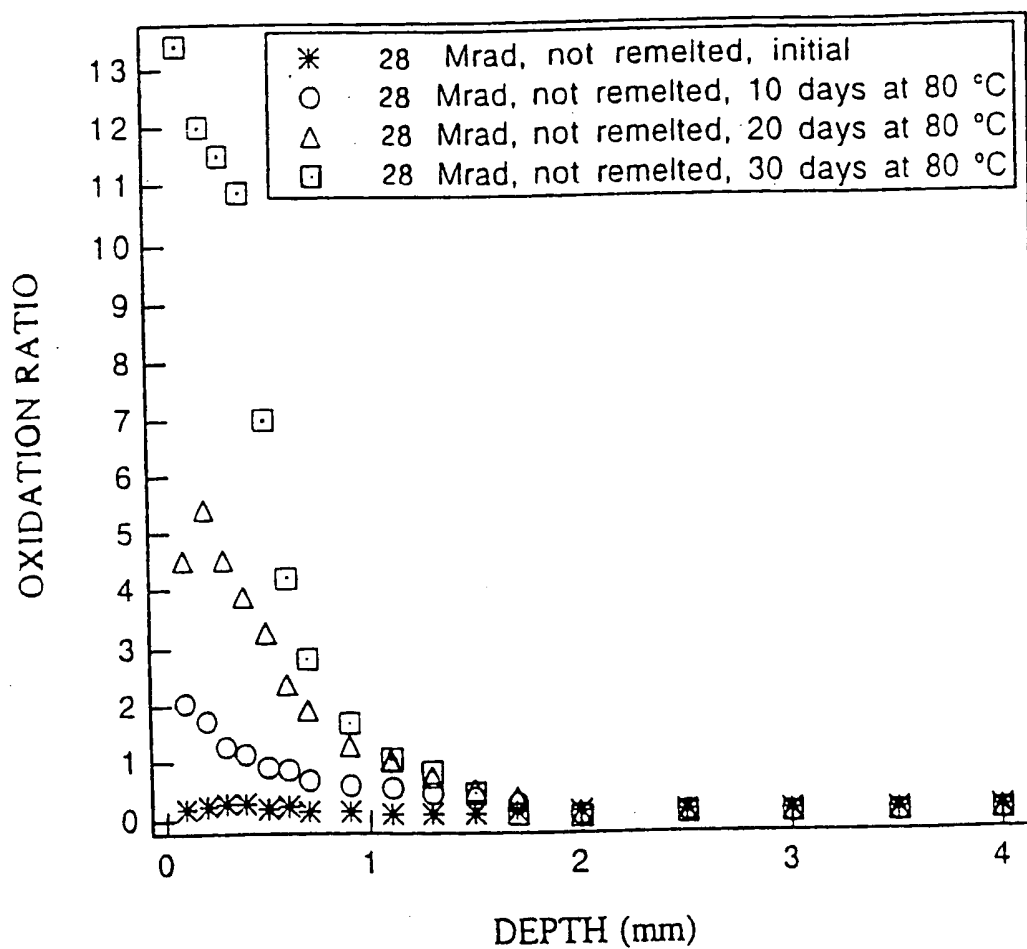


FIG. 12

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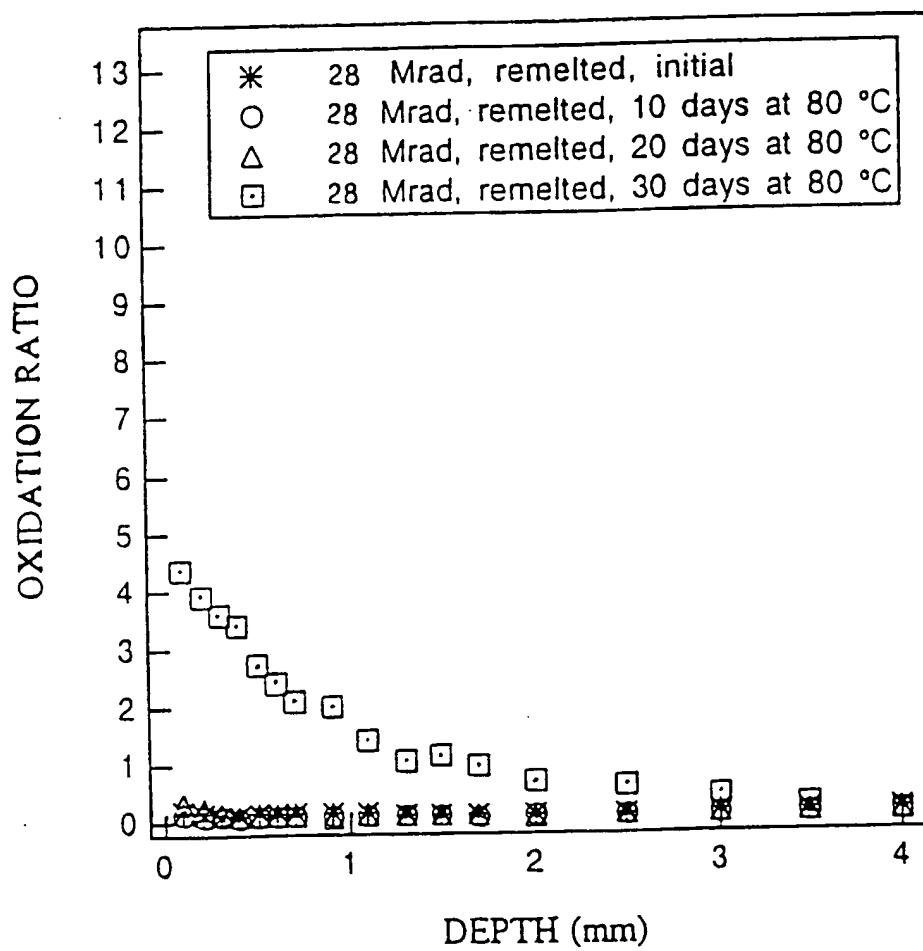


FIG. 13

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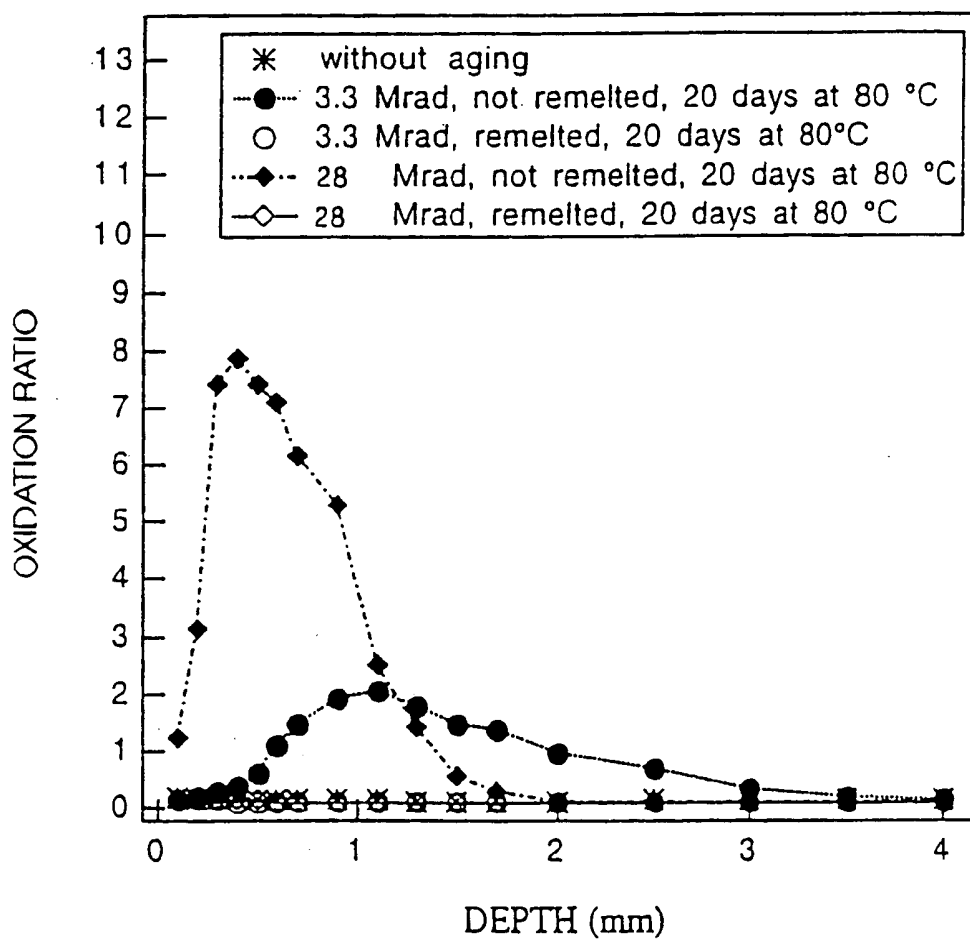


FIG. 14

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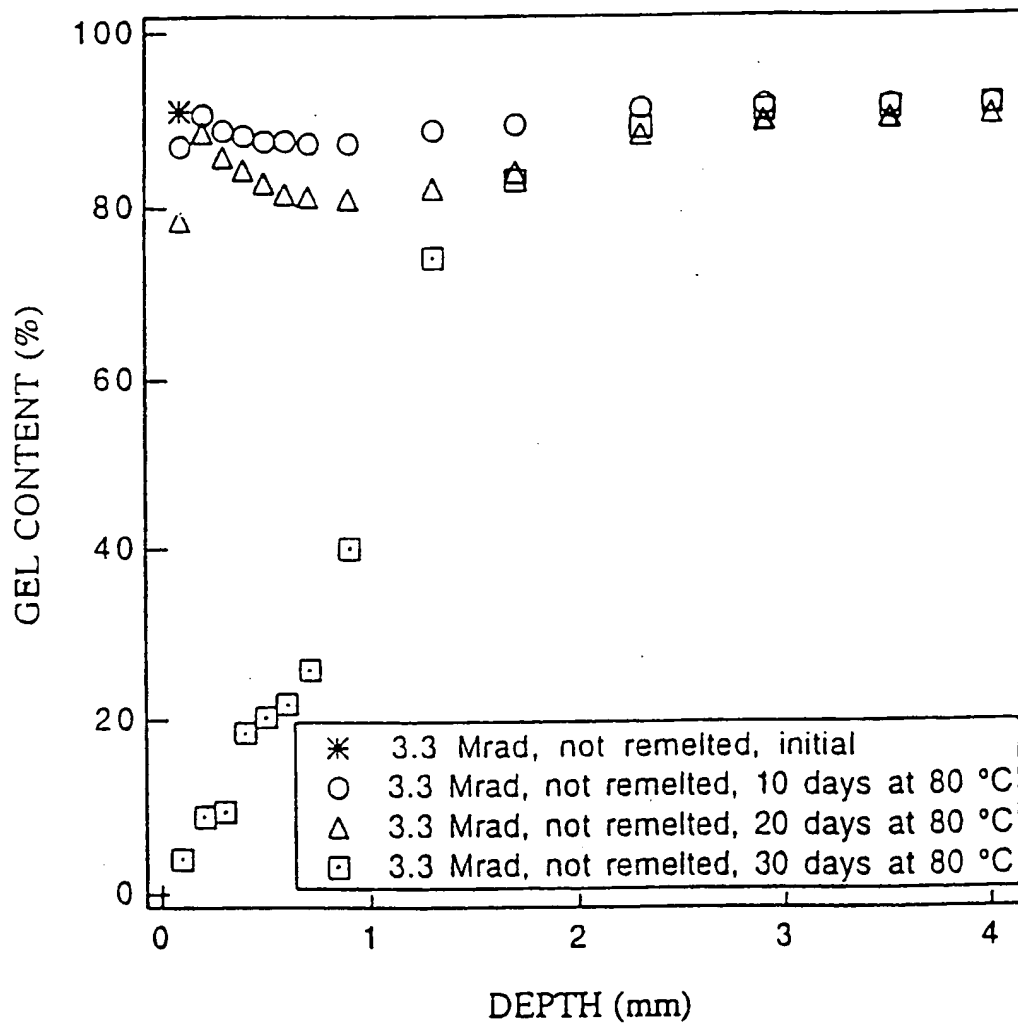


FIG. 15

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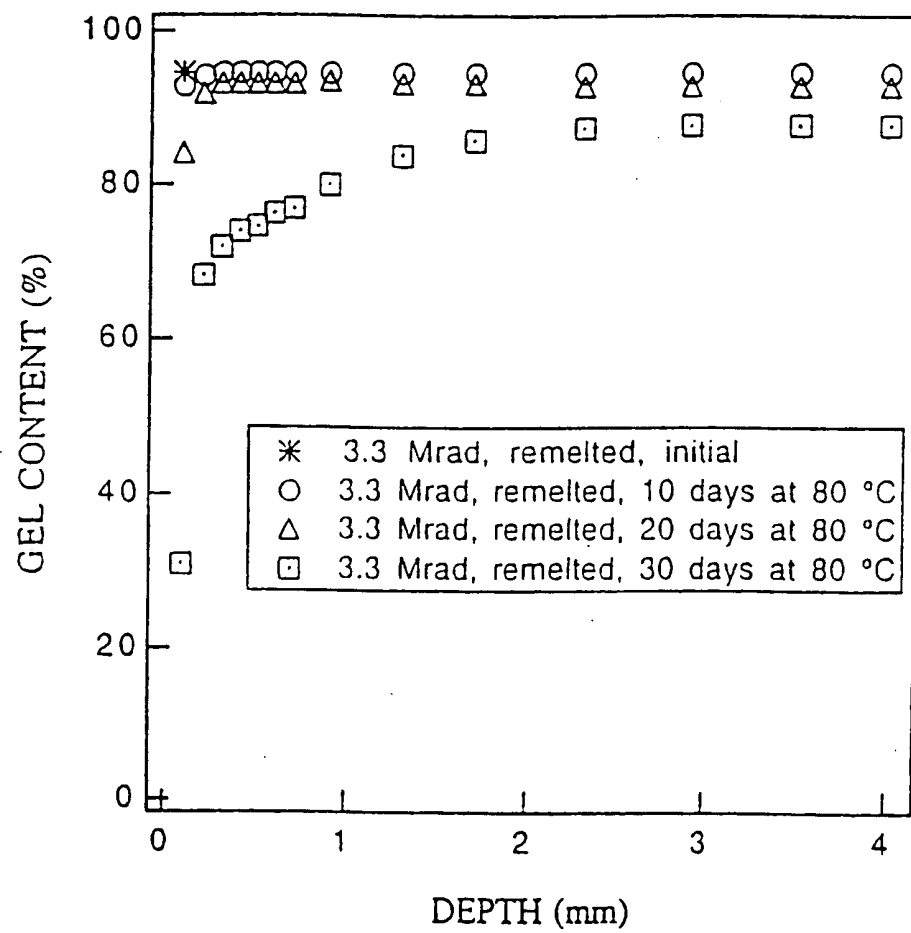


FIG. 16



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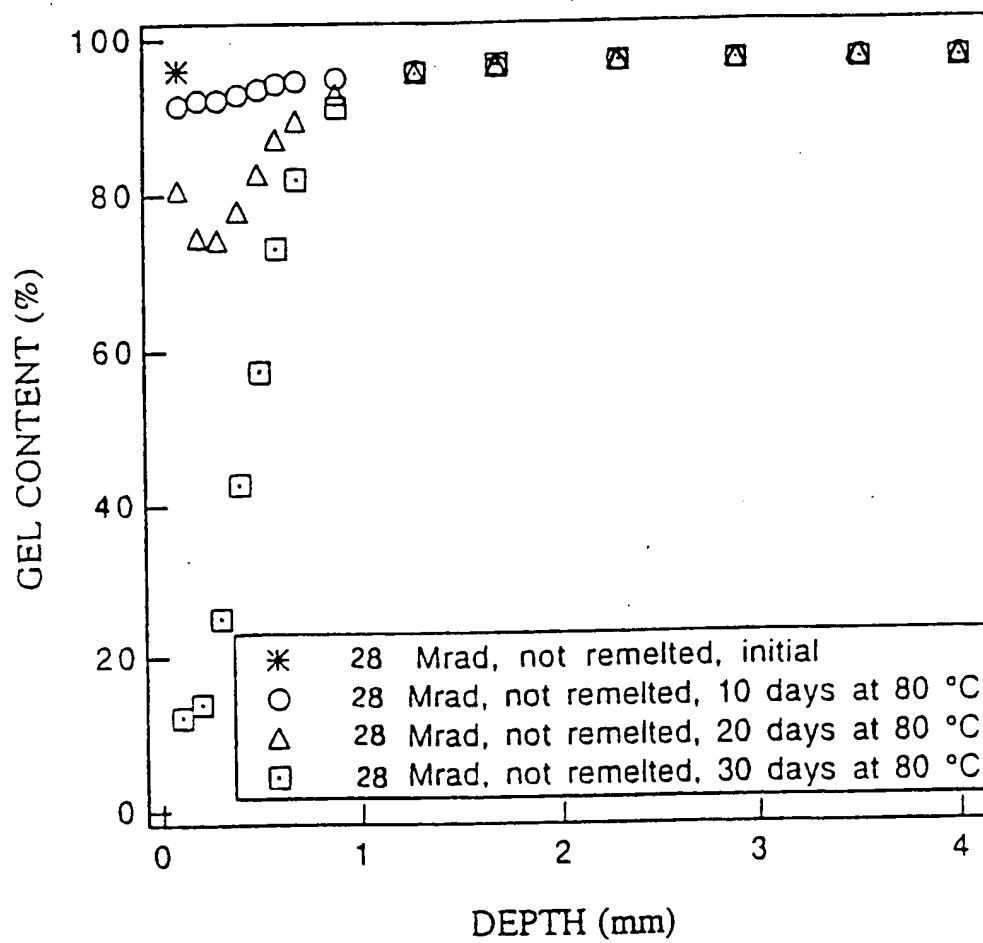


FIG. 17

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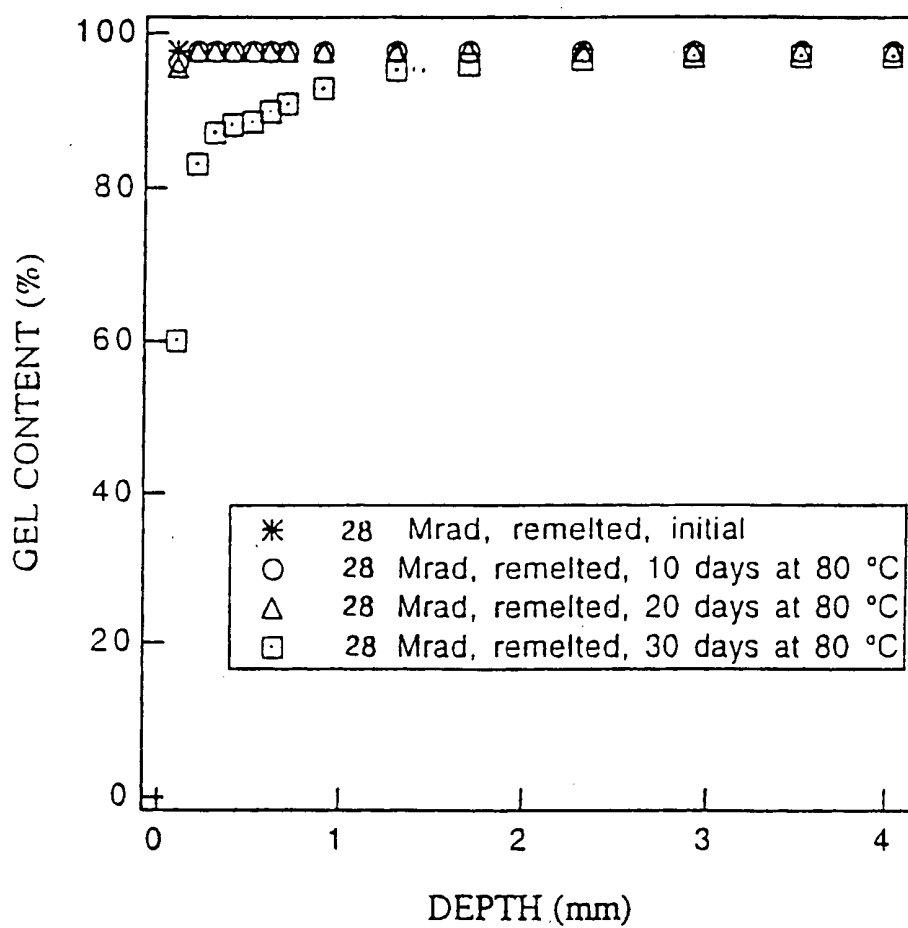


FIG. 18

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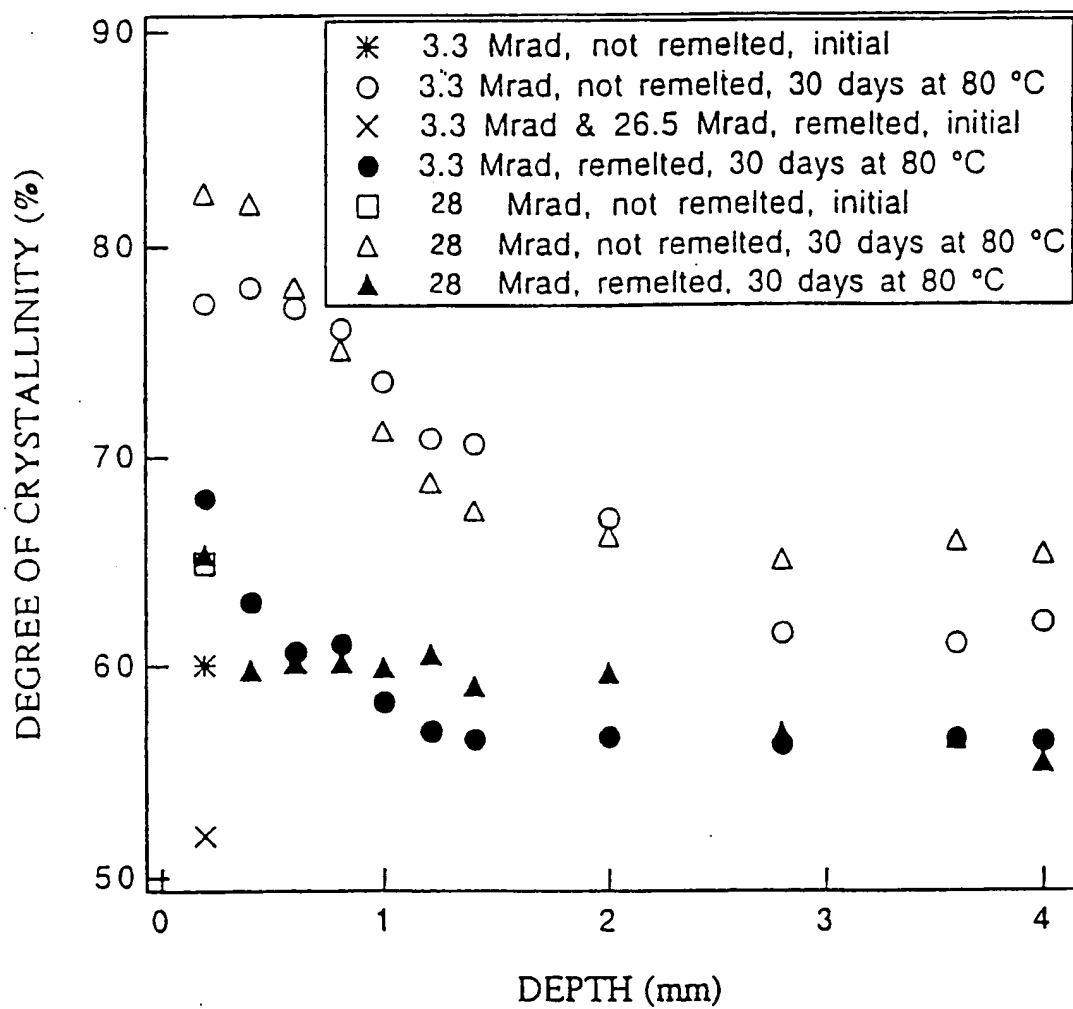


FIG. 19

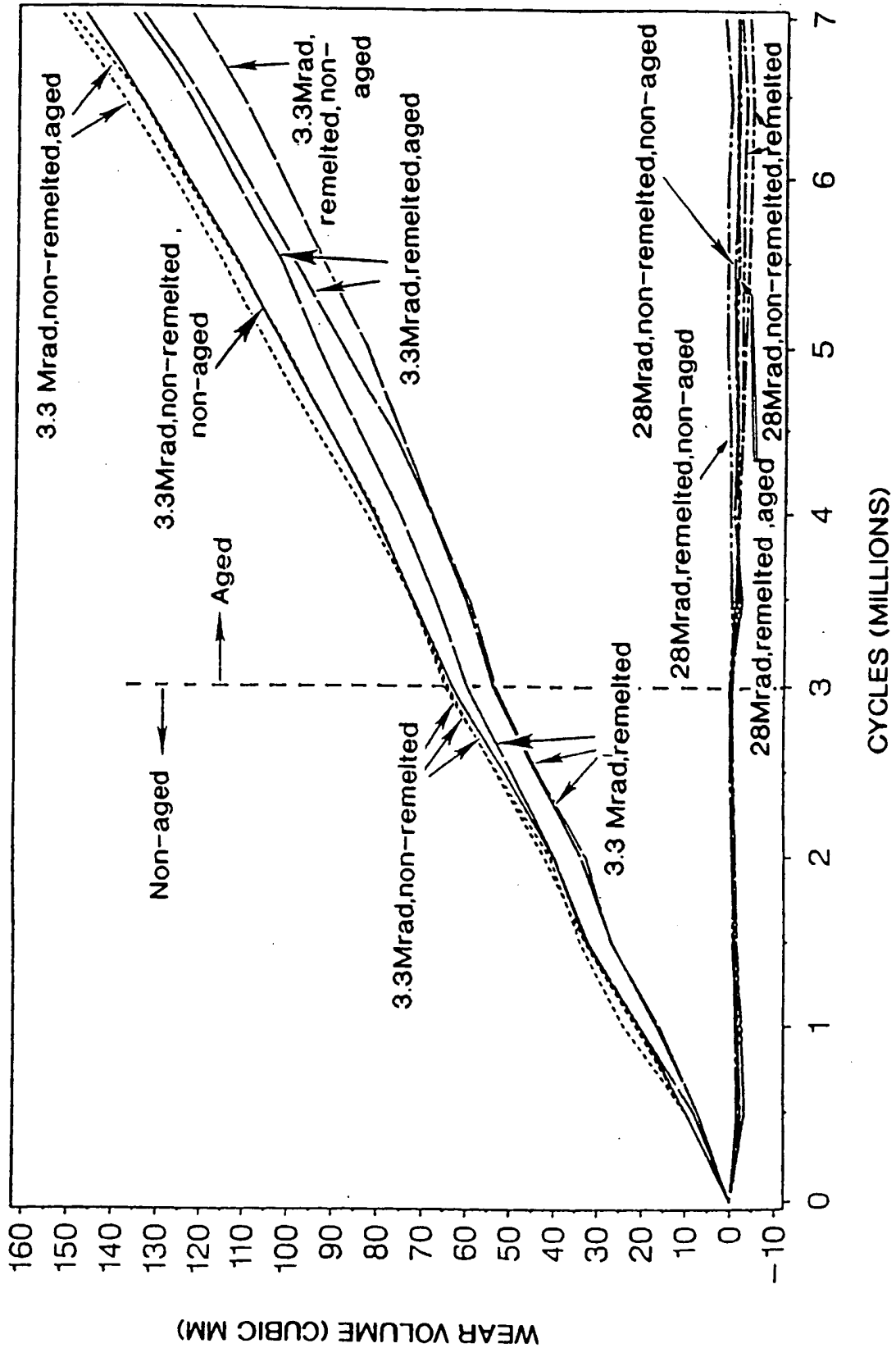


FIG. 20

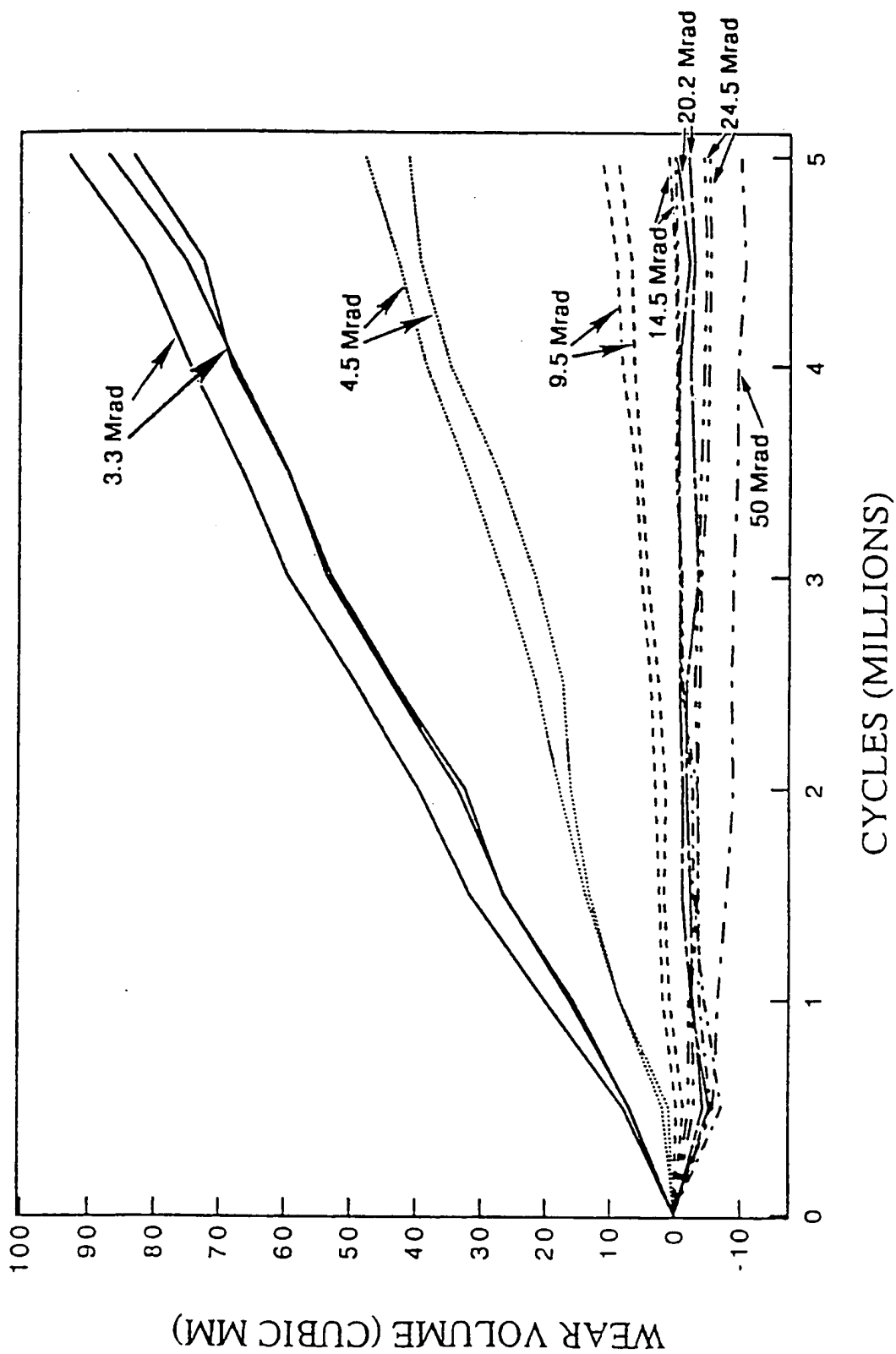
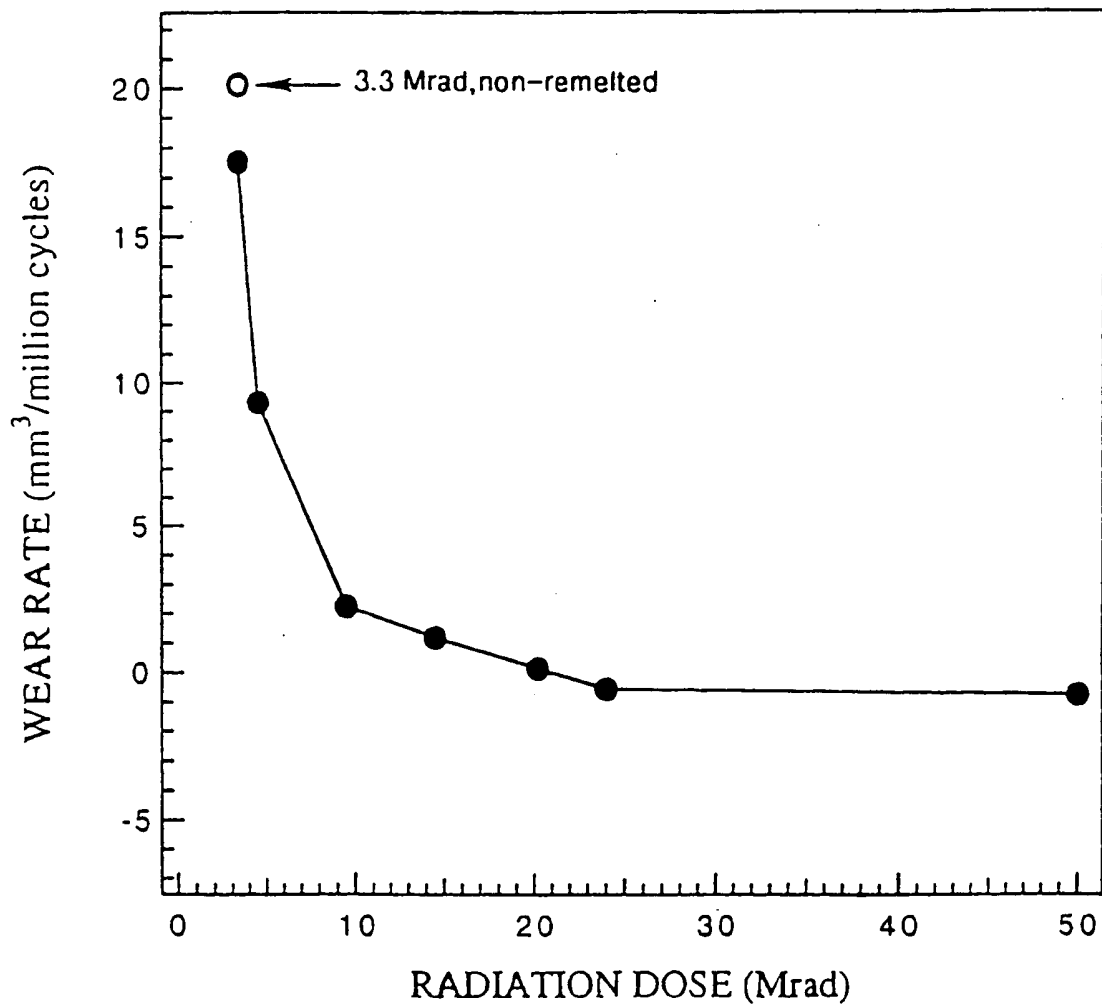


FIG. 21

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**FIG. 22**

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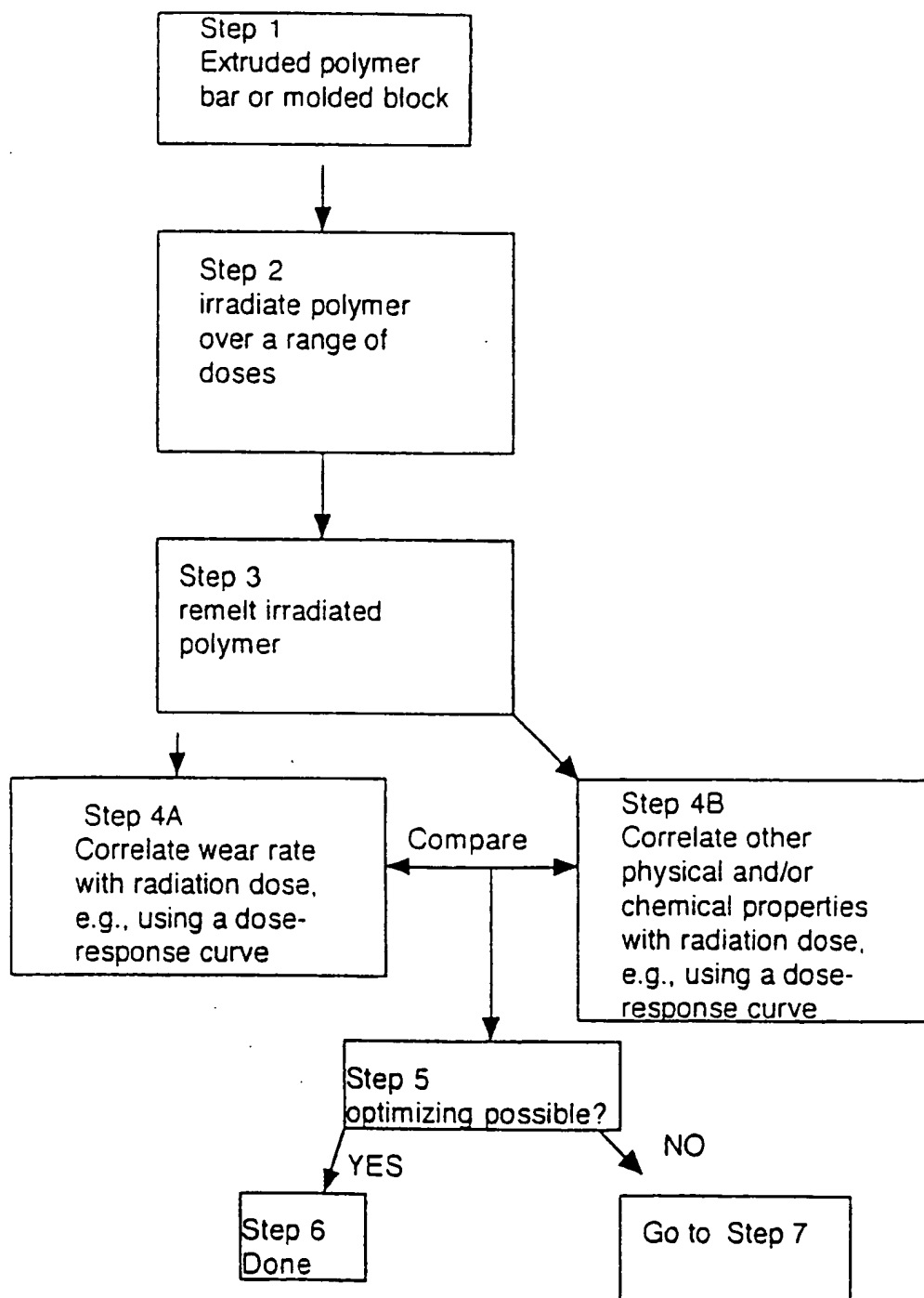


FIG. 23A

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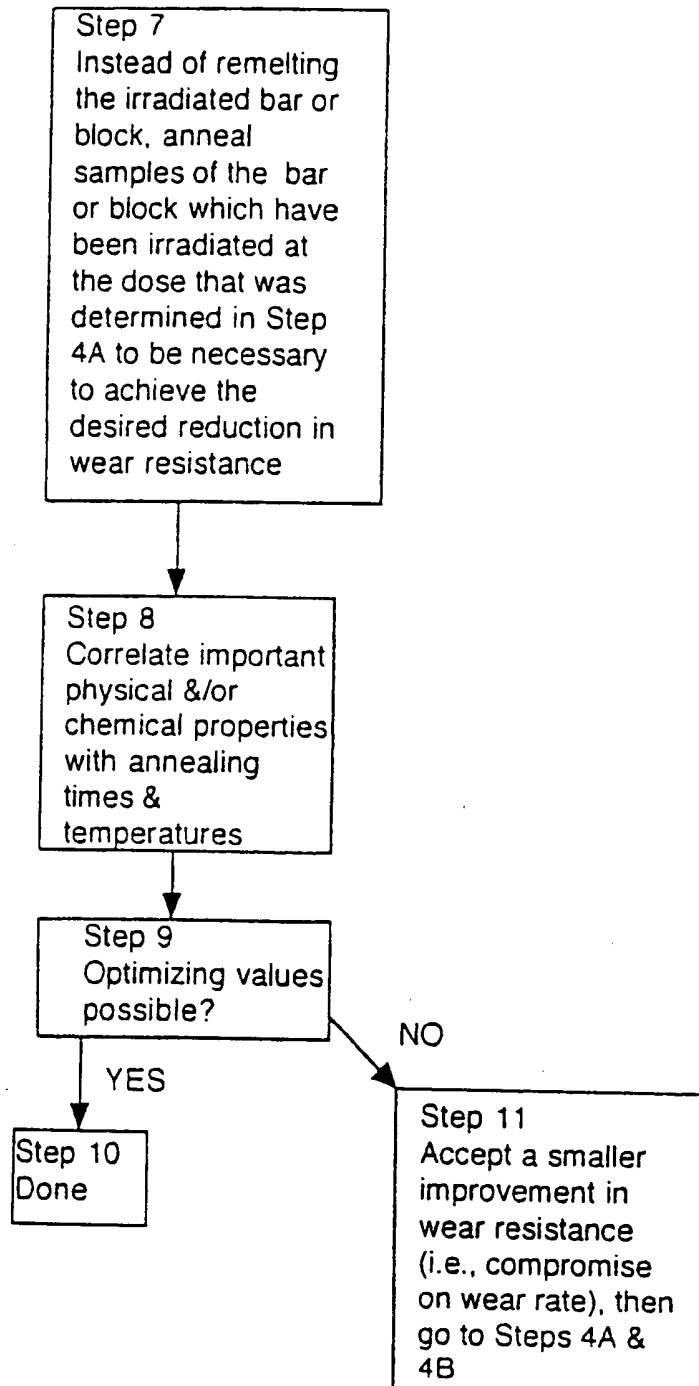


FIG. 23B



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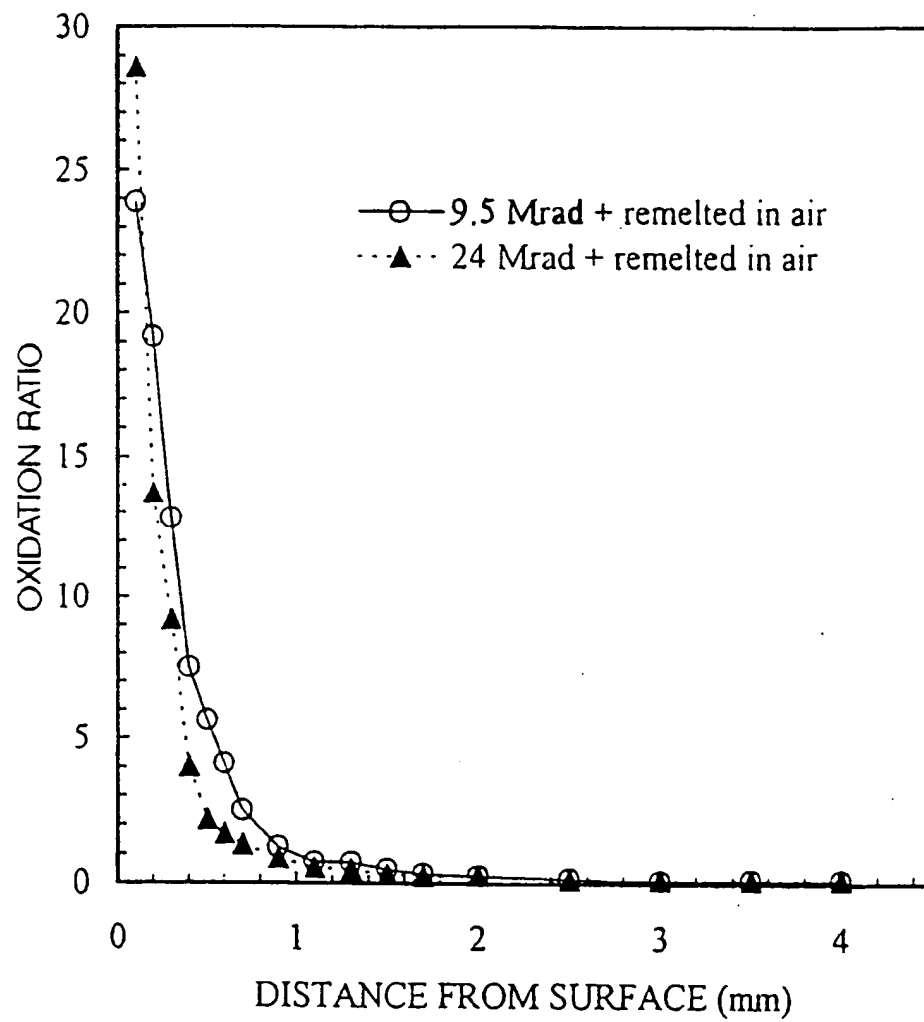
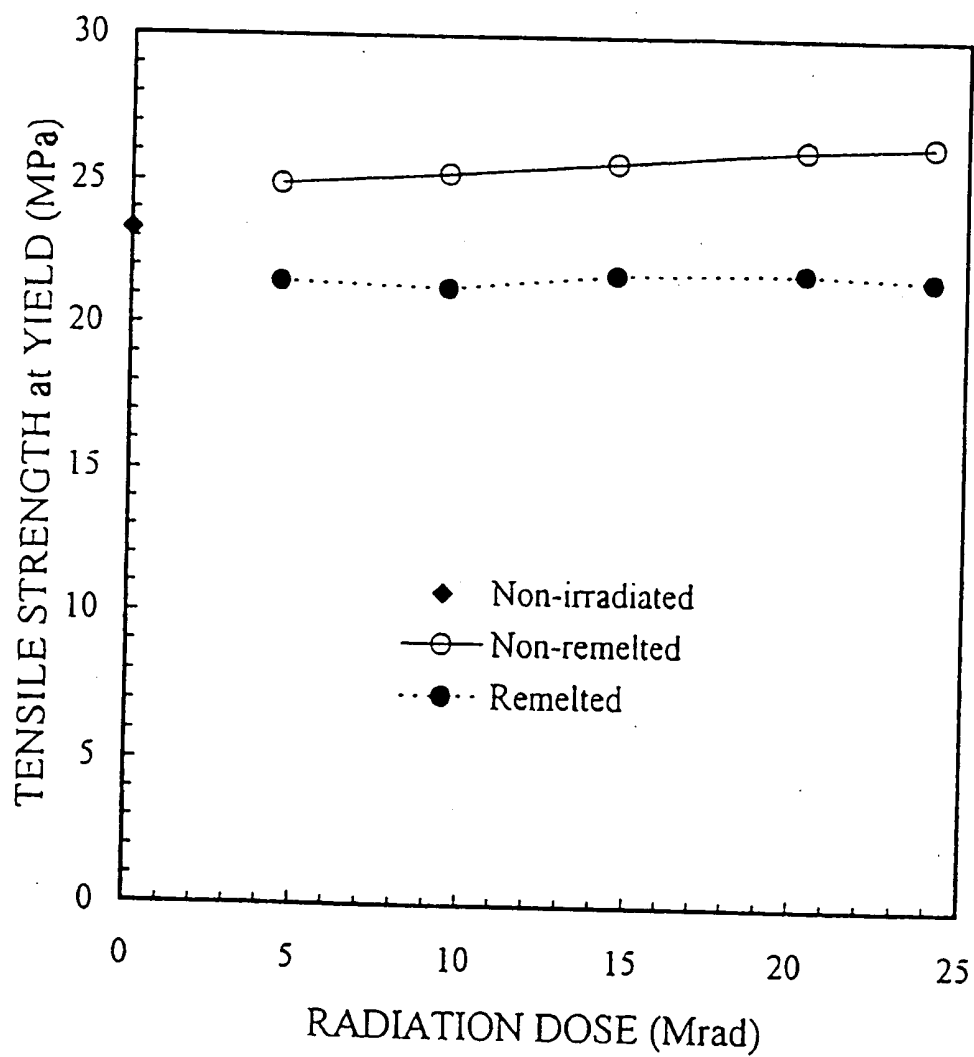


FIG. 24

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**FIG. 25**

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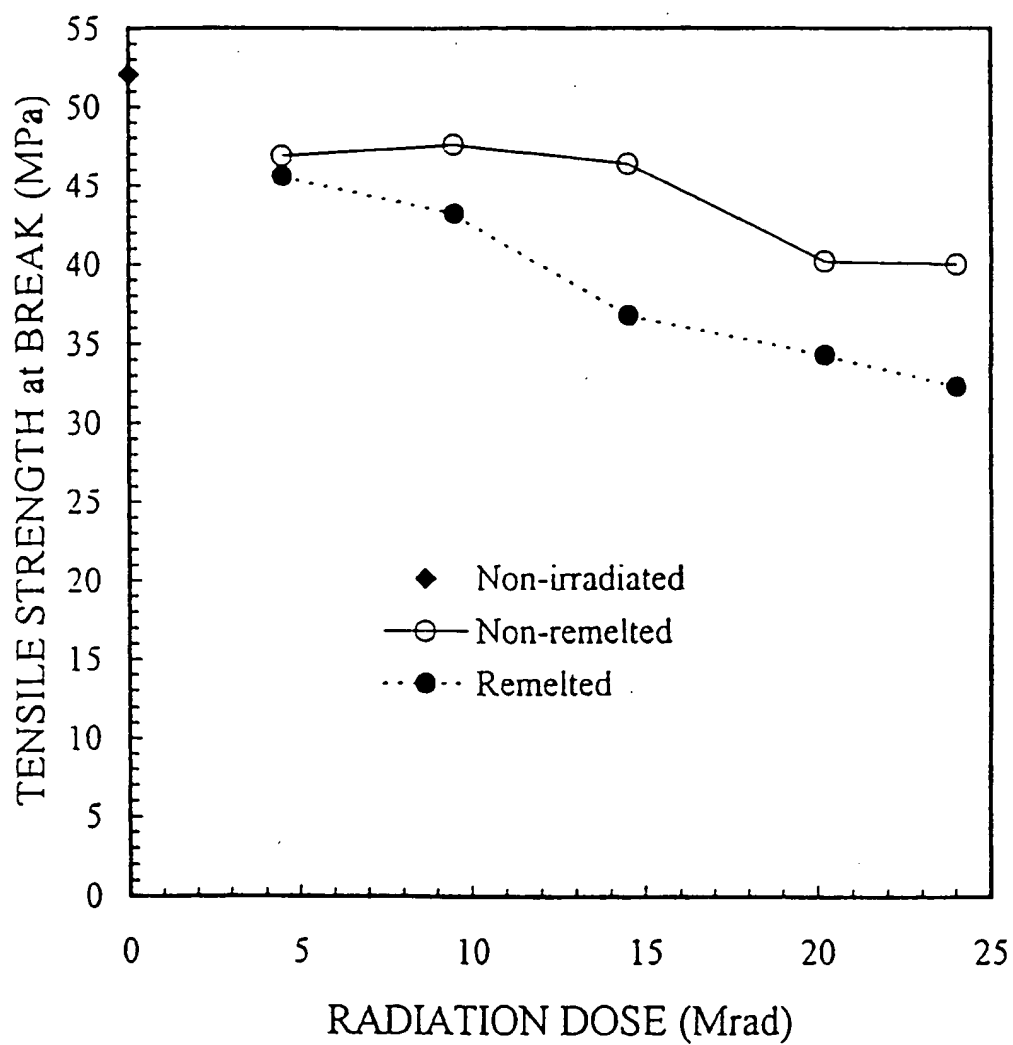


FIG. 26

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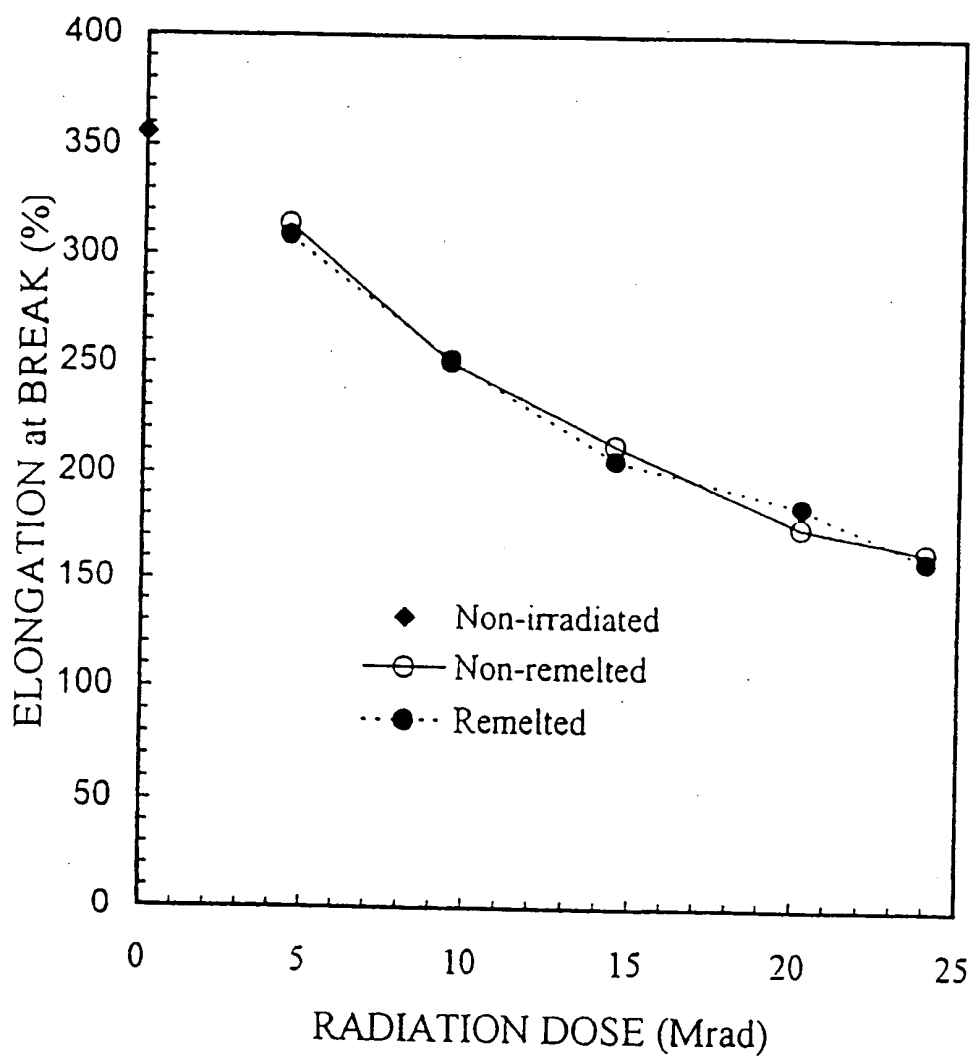


FIG. 27

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US97/11947

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61F 2/00, 2/32, 2/34; C08J 3/28, 5/16; C08F 110/02, 110/06.

US CL : Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 522/153, 161, 163, 164; 523/113, 115; 525/937; 526/351, 352; 623/18, 19, 20, 21, 22, 23.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
noneElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Extra Sheet.

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category*     | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No.  |
|---------------|--|--|
| X<br>---<br>Y | US 4,281,420 A (RAAB) 04 August 1981, Abstract, column 3, lines 19-40, column 5, lines 15-62, column 6, line 34, to column 7, line 11, Examples 2 and 6. | 1, 5-7, 10, 13,<br>15, 16, 21, 23-25,<br>28-30<br>-----<br>2-4, 8, 9, 11, 12,<br>14, 17-20, 22 |
| A             | US 4,055,862 A (FARLING) 01 November 1977, Abstract, column 4, lines 1-51.   | 1-30   |
| X<br>---<br>Y | US 5,439,949 A (LUCAS ET AL) 08 August 1995, column 3, line 41, to column 4, line 34, column 6, lines 1-11, Example 1.                                   | 1, 6, 8, 15, 17,<br>28, 30<br>-----<br>2-5, 7, 9-14, 16,<br>18-27, 29                          |

☒ Further documents are listed in the continuation of Box C.☐ See patent family annex.

\* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*B\* earlier document published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

\*A\* document member of the same patent family

Date of the actual completion of the international search

31 OCTOBER 1997

Date of mailing of the international search report

28 NOV 1997

Name and mailing address of the ISA/US  
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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US97/11947

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category*      | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No.  |
|----------------|---|--|
| Y, P           | US 5,577,368 A (HAMILTON ET AL) 26 November 1996, column 3, lines 35-53, column 4, lines 8-16, column 4, line 63, to column 5, line 4, column 5, lines 39-64, Examples 1-4. | 1-30   |
| Y              | US 5,210,130 A (HOWARD, JR.) 11 May 1993, column 2, line 49, to column 3, line 17, column 5, lines 30-34.   | 1-30   |
| Y              | US 4,582,656 A (HOFFMAN) 15 April 1986, column 1, line 59, to column 2, line 28, Example 1.   | 1-30   |
| X<br>----<br>Y | US 5,200,439 A (ASANUMA) 06 April 1993, column 3, line 27, to column 4, line 5, Examples 1-6.   | 1-4, 6, 8, 9, 12,<br>15, 17, 18, 23,<br>28, 30<br>-----<br>5, 7, 10, 11, 13,<br>14, 16, 19, 24-27,<br>29 |
| X<br>---<br>Y  | US 2,948,666 A (LAWTON) 09 August 1960, column 2, line 55, to column 3, line 23, column 4, lines 47-66, Examples.   | 1, 6, 8, 13, 15,<br>17, 21, 23, 28, 30<br>-----<br>2-5, 7, 9-12, 14,<br>16, 19, 20, 22,<br>24-27, 29     |

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US97/11947

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US97/11947

A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

522/153, 161, 163, 164; 523/113, 115; 525/937; 526/351, 352; 623/18, 19, 20, 21, 22, 23.

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS: prosthetic or artificial joints, acetabular, hip, in vivo implants, bearing surfaces, moving contact, sliding, pivoting, rotating, UHMWPE, HIFAX 1900, GUR 4020, 4120, 4150, polymethylmethacrylate, nylon, polycarbonate, polyethylene, polypropylene, irradiation, photocrosslinking, crystallinity, gel content

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-25, drawn to a thermally treated crosslinked polymer, method of preparing the polymer and in vivo implant comprising the polymer.

Group II, claim(s) 26-30, drawn to a method for determining optimal radiation dose and thermal treatment for treating a polymer and to the product produced.

The inventions listed as Groups I-II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: (1) the steps for determining radiation dose and remelting or annealing conditions set forth in the claims of Group II are not required in the method set forth in the claims of Group I (2) the characteristics of the polymeric composition set forth in the claims of Group I are not mentioned in the claims of Group II.